Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Washington Pharmacy Advisory Committee Meeting

August 18th, 2021

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Agenda Topics

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

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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 – Disease State Description/Guidelines

Tourette's Disorder

- The prevalence of Tourette's disorder is unknown, but observational studies have suggested a prevalence of 1% in school-aged children
- Tourette's disorder is a genetic tic disorder characterized by motor and vocal tics
- Generally, individuals have repetitive, stereotyped movements of vocalizations (e.g., sniffing, muscle tension, blinking)
  - DSM-5 criteria for Tourette's disorder state multiple motor and at least 1 vocal tics are present during the illness (not necessarily simultaneously) and have been present for ≥ 1 year, although they may wax and wane in frequency
- Onset of these symptoms must occur prior to 18 years of age to be considered Tourette's disorder
  - Peak tic severity typically occurs between the ages of 10 and 12 years
- Tics usually improve during adolescence, with 18% of those older than 16 years experiencing no tics and 60% having minimal or mild tics 6 years after initial examination

American Academy of Neurology, 2019

- American Academy of Neurology, 2019
  - No evidence exists demonstrating that treatment is more effective the earlier it is started and watchful waiting is reasonable, especially in those without tic-related functional impairment
  - Comprehensive behavioral intervention for tics (CBIT) may be considered as initial therapy in patients who are motivated to attempt treatment
  - Patients should be assessed for comorbid conditions such as ADHD, OCD, anxiety disorders, oppositional defiant disorder, and mood disorders
  - Alpha-2 adrenergic agonists (e.g., clonidine, guanfacine) may reduce tic severity, particularly in patients with ADHD
  - Regarding other specific pharmacologic agents
    - Haloperidol, risperidone, aripiprazole, and Botox are probably more likely than placebo to reduce tic severity
    - Pimozide, ziprasidone, topiramate, and metoclopramide are possibly more likely than placebo to reduce tic severity
    - Overall, however, there is insufficient evidence to determine the relative efficacy of these drugs
  - Notably, a higher risk of drug-induced movement disorders is associated with haloperidol, pimozide, and risperidone and with long-term use of metoclopramide
  - Patients with severe Tourette syndrome resistant to medical and behavioral therapy may benefit from deep brain stimulation (DBS)

Antipsychotics

- **olanzapine/samidorphan (Lybalvi)**
  - **June 2021: FDA has approved olanzapine/samidorphan (Lybalvi), a combo of an atypical antipsychotic and an opioid antagonist, indicated for the treatment of 1) schizophrenia in adults and 2) bipolar I disorder in adults for the acute treatment of manic or mixed episodes as monotherapy and as adjunct to lithium or valproate as well as for maintenance monotherapy treatment**
  - **Indication**
    - **Indicated for the treatment of:**
      - **Schizophrenia in adults**
      - **Bipolar I disorder in adults: Acute treatment of manic or mixed episodes as monotherapy and as adjunct to lithium or valproate; Maintenance monotherapy treatment**
  - **Warnings**
    - **BBW: Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Lybalvi is 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)**
    - **Precipitation of Opioid Withdrawal in Patients Who are Dependent on Opioids: Can precipitate opioid withdrawal in patients who are dependent on opioids. Prior to initiating therapy, there should be at least a 7-day opioid-free interval from the last use of short-acting opioids, and at least a 14-day opioid-free interval from the last use of long-acting opioids to avoid precipitation of opioid withdrawal**
  - **Dosage**
    - **Stratified by indication**
  - **Availability**
    - **Tablets (olanzapine/samidorphan): 5 mg/10 mg, 10 mg/10 mg, 15 mg/10 mg and 20 mg/10 mg**

Antipsychotics

- **Discontinuations**
  - **fluoxetine/olanzapine (Symbyax) – July 2020**
    - **Eli Lilly will discontinue Symbyax 6/50 mg and 12/50 mg capsules**
    - **Distribution will continue until end of December 2020**
  - **asenapine maleate (Saphris) – February 2021**
    - **Allergan has made a business decision to discontinue the 5 mg sublingual tab presentation packaged in a box of 100 (10 blisters with 10 tabs) and the 10 mg sublingual tablet packaged in a box of 100 (10 blister with 10 tablets**
    - **All other packaging configurations continue to be available**

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Cytokine and CAM Antagonists:

Cytokine & CAM Antagonist - Disease State Description

- Cytokines and cell-adhesion molecules (CAMs) are chemical mediators involved in inflammatory processes throughout the body

Cytokines

- Small proteins secreted in response to an immune stimulus for the purpose of mediating and regulating immunity, inflammation, and hematopoiesis
- Derived from monocytes and macrophages and induce gene expression of a number of proteins that contribute to the inflammatory response
- The actions of the individual cytokines are widely varied and they contribute to fibrosis and tissue degeneration associated with chronic inflammation, primarily by inducing the proliferation of fibroblasts and collagenase
- The pro-inflammatory cytokines, tumor necrosis factor (TNF), and interleukin (IL)-1, are involved in tissue destruction in many chronic inflammatory diseases affecting various organs
  - TNFα also has a role in Crohn's disease in stimulation of inflammation

European Respiratory Journal, 2003

Cytokine & CAM Antagonist - Disease State Description

Cell Adhesion Molecules (CAM)

- Cell surface proteins involved in the binding of cells, usually leukocytes, to each other, endothelial cells, or the extracellular matrix
- Specific signals produced in response to wounds and infection control the expression and activation of these molecules
- Most of the CAMs characterized fall into 3 general families of proteins:
  - The immunoglobulin (Ig) superfamily
    - The adhesion molecules that bind to integrins on leukocytes and mediate their flattening onto the blood vessel wall
  - The integrin family
    - Consists of an α chain and a ß chain that mediate cell-to-cell interactions, such as leukocyte adherence to the vascular endothelium
  - The selectin family
    - Involved in the adhesion of leukocytes to activated endothelium followed by extravasation through the blood vessel walls into lymphoid tissues and sites of inflammation
  - Other proteins that are functionally classified as CAMs are involved in strengthening the association of T cells with antigen-presenting cells or target cells, in T cell activation, and in recirculating lymphocytes back to the circulation via the lymphatic system
- Different CAMs have been implicated in inflammatory, fibrotic, and autoimmune diseases

European Respiratory Journal, 2003

Juvenile Idiopathic Arthritis - Treatment Guidelines

ACR/Arthritis Foundation, 2019

- The organization recommends nonsteroidal anti-inflammatory drugs (NSAIDs) conditionally as adjunctive therapy (very low level of evidence)
- Regarding traditional DMARDs for polyarthritis
  - **Methotrexate is conditionally recommended over leflunomide or sulfasalazine** (moderate and very low evidence, respectively)
  - **Subcutaneous (SC) methotrexate is conditionally recommended over oral methotrexate** (very low evidence)
- For biologic DMARDs in patients with polyarthritis
  - **Combination therapy with a DMARD is conditionally recommended over biologic monotherapy when initiating treatment with a biologic** (etanercept [very low evidence], adalimumab [moderate evidence], golimumab [very low evidence], abatacept [low evidence], or tocilizumab [low evidence])
- Combination therapy with a DMARD is strongly recommended for infliximab (low evidence)
- Intraarticular glucocorticoids are conditionally recommended as adjunct therapy (very low evidence), and oral corticosteroids as a bridge therapy are conditionally recommended in patients with moderate or high disease activity (very low evidence); however, bridge therapy is not recommended in patients with low disease activity (very low evidence)
- In addition, the group strongly recommends against adding chronic low-dose glucocorticoids, regardless of disease activity (very low evidence) in polyarthritis patients

Juvenile Idiopathic Arthritis - Treatment Guidelines

ACR/Arthritis Foundation, 2019

- For initial therapy in polyarthritis patients
  - The group strongly recommends **all patients have initial therapy with DMARD over NSAID monotherapy** (moderate evidence), with methotrexate monotherapy conditionally recommended over triple DMARD therapy (low evidence)
- In patients without risk factors (e.g., positive anti-cyclic citrullinated peptide antibodies, positive rheumatoid factor, or presence of joint damage)
  - The group recommends **initial therapy with a DMARD conditionally over a biologic** (low evidence); however, in those with risk factors, the group recognizes that there are situations in which a biologic may be preferred (low evidence; e.g., involvement of high risk joints [cervical spine, wrist, or hip], high disease activity, and or those judged to be high risk of disabling joint damage)
- For subsequent therapy in low disease activity patients, defined as clinical Juvenile Disease Activity Score based on 10 joints (cJADAS-10) ≤ 2.5 and ≥ 1 active joint
  - **Escalation of therapy** (e.g., intraarticular glucocorticoid injection, DMARD dose optimization, methotrexate trial, and adding or changing biologic) is recommended over no escalation (very low evidence)
  - For **subsequent therapy in moderate or high disease activity** (cJADAS-10 > 2.5) **patients receiving DMARD monotherapy**, the group conditionally recommends **adding a biologic to the original DMARD over changing to a second DMARD** (low evidence) or **triple DMARD therapy** (low evidence)
  - For **subsequent therapy in moderate or high disease activity polyarthritis patients receiving a TNF antagonist with or without a DMARD**, the group conditionally recommends **switching to a non-TNF antagonist** (e.g., tocilizumab, abatacept) over switching to a second TNF antagonist (very low evidence); **however, a second TNF antagonist may be appropriate in patients with good initial response to a TNF antagonist who have experienced secondary failure**
  - If the patient is receiving their second biologic, **use of a TNF antagonist, abatacept, or tocilizumab is conditionally recommended over rituximab** (very low evidence)

Juvenile Idiopathic Arthritis - Treatment Guidelines

ACR/Arthritis Foundation, 2019

- For patients with JIA and sacroiliitis
  - Guidelines strongly recommends treatment with an **NSAID over no NSAID treatment** (very low evidence)
  - In those who are **already on NSAIDs with continued active disease, the group strongly recommends a TNF antagonist over NSAID monotherapy** (low evidence), with a conditional recommendation (low evidence) for sulfasalazine in those who have contraindications or have failed a TNF antagonist
  - The group strongly **recommends against the use of methotrexate monotherapy** (very low evidence)
  - **Bridging therapy with a limited duration oral corticosteroid in select conditions and adjunct use of intraarticular glucocorticoid are conditionally recommended** (both very low evidence)
  - For those with **JIA and enthesitis**, the group strongly recommends **NSAID treatment over no NSAID treatment** (very low evidence), **with a TNF antagonist conditionally recommended over methotrexate or sulfasalazine** if disease activity continues (low evidence)
  - Bridging therapy with a **limited duration oral corticosteroid** in select conditions also is conditionally recommended (very low evidence)
  - The group provides additional recommendations on specific glucocorticoids

Pediatric Psoriasis - Treatment Guidelines

American Academy of Dermatology and National Psoriasis Foundation, 2019

- Published guidelines for management and treatment of psoriasis (PSO) in pediatrics
  - Recommend ongoing assessment for psoriatic arthritis (PsA), uveitis, obesity, CV risk factors, dyslipidemia, insulin resistance/diabetes, mental health conditions
  - Body surface area (BSA) plus Children's Dermatology Life Quality Index should be used to assess disease severity

- **Treatment**:
  - Recommended topical treatments for PSO include:
    - Topical corticosteroids (off-label), tacrolimus 0.1% ointment (off-label) for PSO of face and genital region, calcipotriene/calcipotriol, calcipotriol/betamethasone dipropionate (ages ≥ 12 yo), tazarotene (off-label) + topical corticosteroids, topical anthralin, coal tar, phototherapy/photochemotherapy
  - Recommended systemic treatments for PSO include:
    - Systemic treatments include methotrexate, cyclosporine, systemic retinoids, and biologics, etanercept, infliximab, adalimumab, and ustekinumab
  - Lastly, guidelines recommend treatment of physical and psychosocial wellness (quality of life) in pediatric patients with PSO

Ankylosing Spondylitis – Background and Guidelines

Background:

- Axial spondyloarthritis (axSpA) is an inflammatory condition generally affecting the spine and can be furthered subdivided into ankylosing spondylitis (AS; radiographic axSpA) and nonradiographic axSpA (nr-axSpA

American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network

- Published a 2019 update on the treatment of ankylosing spondylitis (AS) and nonradiographic axial spondyloarthritis (SpA)
- In general, recommendations for AS and nonradiographic axial SpA are similar
- TNF antagonists (but not a specific one) are recommended as first biologic (over Cosentyx or Tremfya, which are then recommended over a second TNF antagonist if first does not produce a response)
- All the prior mentioned agents are recommended over Xeljanz
- Concurrent low-dose methotrexate with TNF antagonist is not recommended
- Recommend against a strict treat-to-target strategy
- If a patient's disease is stable, guidelines recommend against discontinuing or tapering of biologics
- Sulfasalazine provides a viable option for select patients who cannot take a TNF antagonist

Periodic Fever Syndrome - Background and Guidelines

Background:

- These rare, hereditary syndromes are characterized by short and recurrent severe localized inflammation and fever "attacks" that are not otherwise explained by routine childhood (or adult) infections
- Periodic fever syndrome is defined as 3 or more episodes of unexplained fever in a 6-month period, occurring at least 7 days apart
    - These can occur periodically or irregularly and undergo spontaneous remission
- Cryopyrin-associated periodic syndromes (CAPS) is a family of syndromes associated with mutations in cryopyrin, now known as nucleotide-binding domain and leucine-rich repeat containing family, pyrin domain-containing 3 (NLRP2)
    - CAPS includes Muckle-Wells syndrome (MWS), familial cold autoinflammatory syndrome (FCAS), and chronic infantile neurologic cutaneous articular syndrome (CINCA), which is also known as neonatal-onset multisystem inflammatory disease (NOMID)

Treatment:

- Anakinra (Kineret), canakinumab (Ilaris), and rilonacept (Arcalyst) are approved for the treatment of CAPS in select ages
- Kineret is only approved for patients with CAPS associated with NOMID
- Arcalyst and Ilaris are approved more generally for patients with CAPS, including FCAS and MWS
    - Ilaris is also approved for the following other periodic fever syndromes:
        - Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS), Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD), and Familial Mediterranean Fever (FMF)

Giant Cell Arteritis (GCA) - Background and Guidelines

- **Background**:
  - GCA, or temporal arteritis, is a systemic inflammatory vasculitis of unknown etiology that is classified as a large-vessel vasculitis, but typically also involves small and medium arteries
  - Most commonly, it affects the occipital, ophthalmic, posterior ciliary, proximal vertebral, and vertebral arteries
    - While the incidence of GCA ranges from 0.5 to 27 cases per 100,000 people in those ≥ 50 years old, the incidence is higher in the northern areas of the U.S
    - It occurs in older persons and can result in a wide variety of neurologic, ophthalmologic, and systemic complications

- **Treatment**:
  - High-dose corticosteroids, although clinical studies on various dosing protocols are limited
  - Steroids are generally continued until the resolution of symptoms and then may be tapered slowly to the lowest dose that adequately suppresses symptoms
  - Actemra is the only non-corticosteroid drug FDA approved for the treatment of GCA

Hidradenitis Suppurativa - Background and Guidelines

Hidradenitis Suppurativa (HS)

- HS is a chronic condition that affects the terminal follicular epithelium in apocrine gland-bearing skin, such as the armpits or perianal area
- It typically occurs in adolescents (generally after puberty) and adults, is generally diagnosed clinically, and affects approximately 1% to 2% of the U.S. population
- Select signs and symptoms include erythema, raised bumps or lesions, painful lesions, and local arthritis or arthralgia
- In addition to nonpharmacologic treatments, pharmacologic treatment includes anti-inflammatories, antibiotics, antiandrogens, and biologics, such as infliximab (Remicade)
    - Surgery may also be considered in some patients

- **European Dermatology Forum, 2015**
    - Guidelines for treatment are limited, but guidelines from the European Dermatology Forum recommend either adalimumab or infliximab in severe or refractory disease, stating adalimumab appears to be better tolerated; however, only adalimumab is approved by the FDA for this use

Uveitis

- Non-infectious intermediate and posterior uveitis is inflammation of the intermediate and posterior uvea, while panuveitis is inflammation of the anterior chamber, vitreous humor, and choroid or retina simultaneously
- Together, these represent the most severe and highly recurrent forms of uveitis
- The incidence of all cases of uveitis is approximately 15 cases per 100,000 patients per year, and anterior uveitis is the most common form of uveitis

Uveitis – Guidelines

Uveitis (Treatment)

- ACR and Arthritis Foundation, 2019
  - Published guidelines on the treatment of uveitis associated with JIA, one of the most common extraarticular manifestation of JIA
  - The group recommends select topical glucocorticoids in patients with JIA and active chronic anterior uveitis for short-term control, but for those who are unable to control symptoms with short-term therapy, they recommend adding systemic therapy in order to taper topical glucocorticoids
    - Changing or escalating systemic therapy is recommended after ≥ 3 months if control is not achieved
  - For JIA patients who develop new chronic anterior uveitis despite stable systemic therapy, they recommend topical glucocorticoids prior to changing or escalating systemic therapy right away
  - Regarding specific agents, they group recommends SC methotrexate conditionally over oral methotrexate; however, use of a TNF antagonist with methotrexate in severe active disease and sight-threatening complications is conditionally recommended over methotrexate monotherapy
  - If starting a TNF antagonist, they conditionally recommend a monoclonal antibody over etanercept
    - Dose or frequency of the TNF antagonist should be escalated for an inadequate response prior to trying another biologic agent
    - Likewise, if a patient has failed a TNF antagonist following an escalated dose/frequency, changing to a different TNF antagonist is conditionally recommended over another biologic
  - Abatacept or tocilizumab as biologics and mycophenolate, leflunomide, or cyclosporine as nonbiologic options are conditionally recommended in patients who have failed methotrexate and 2 monoclonal antibody TNF antagonists
  - The disease should be well-controlled for 2 years on a DMARD and/or biologic therapy prior to tapering
  - For pediatric patients with spondyloarthritis who develop acute anterior uveitis, the group conditionally recommends topical glucocorticoids prior to a change in systemic therapy
  - Notably, the only agent approved for uveitis in this class is adalimumab

Cytokine & CAM Antagonist - Background and Guidelines

Cytokine Release Syndrome (CRS)

- CRS can occur following select immunotherapies and can result in a large, rapid release of cytokines into the blood
- This can manifest as fever, nausea, headache, rash, tachycardia, hypotension, and dyspnea and can be life-threatening
- Tocilizumab (Actemra) is approved for the treatment of chimeric antigen receptor (CAR) T cell-induced severe or life-threatening CRS in adults and pediatric patients 2 years of age and older

Role of Biosimilars

- In 2017, the ACR published a white paper regarding the use of biosimilars in the treatment of rheumatic diseases and provides a comprehensive overview of the scientific, clinical, economic, and prescribing issues pertaining to biosimilar use, including efficacy and competition
- They note that available real-world studies have demonstrated efficacy for extrapolated indications and state that health care providers should incorporate biosimilars, where appropriate, into treatment for patients with rheumatologic diseases
- An international multidisciplinary task force issued consensus-based recommendations on the use of biosimilars for rheumatologic diseases, focusing on multiple factors, including extrapolation of indications, and switching between originator products and biosimilars
- They state treatment is a shared decision between the patient and clinician, and patients and providers must be educated on biosimilars
- In addition, biosimilars are not considered superior or inferior to the originator product, and biosimilars should be considered safe and effective for all the originator product's approved indications
- Notably, ACR cautions against interchangeability without consultation with a prescriber

Ulcerative Colitis – Disease State Description

- Ulcerative colitis (UC) is a chronic inflammatory disease primarily affecting the colon and rectum
- UC affects approximately 1,000,000 people in the United States (US) and the incidence continues to increase worldwide. The Center for Disease Control and Prevention (CDC) estimates the current prevalence of UC at 238 per 100,000 adults
  - UC may present at any age, but onset typically peaks between 15 and 30 years of age
- The disease is characterized by superficial infiltration of the bowel wall by inflammatory white cells, resulting in multiple mucosal ulcerations and crypt abscesses
- The predominant symptom of UC is diarrhea, which is usually associated with blood in the stool
  - Additional symptoms may include pain in the lower quadrant or rectum along with systemic features, including fever, malaise, and weight loss (which are more common if a greater portion of the colon is affected)
  - The initial attack of UC may be fulminant with bloody diarrhea, but the disease more commonly begins indolently, with non-bloody diarrhea progressing to bloody diarrhea
  - UC can present initially with any extent of anatomic involvement ranging from disease confined to the rectum to the entire large intestine (pancolitis)
  - Most commonly, UC follows a chronic intermittent course with long periods of quiescence interspersed with acute attacks lasting weeks to months. However, a significant percentage of patients suffer a chronic continuous course

Centers for Disease Control and Prevention, 2015

Treatment Guidelines

American Gastroenterology Association (AGA), 2020

- Moderate to severe UC considers patients with moderate to severe disease to be those who are dependent on or refractory to corticosteroids, exhibit ulcers upon endoscopic assessment, or are at high risk for colectomy
- Long-term management can include medications from the following classes:
  - TNF-alpha antagonists, immunomodulators (e.g., thiopurines [azathioprine], methotrexate), the anti-integrin agent vedolizumab, and JAK inhibitors (e.g., tofacitinib)
  - If the agent selected for inducing remission is effective, it is usually continued as maintenance therapy; the exception to this would be when corticosteroids or cyclosporine are used for induction of remission
  - The following agents are recommended over no treatment for adult outpatients with moderate to severe UC, listed in order of FDA approval: infliximab, adalimumab, golimumab, vedolizumab, tofacitinib, or ustekinumab
  - In patients who are biologic-naive, infliximab or vedolizumab are suggested rather than adalimumab for induction of remission; however, patients with less severe disease who value the convenience of self-administration over the relative efficacy of therapy may select adalimumab instead
  - For induction of remission, thiopurine monotherapy is suggested against use; however, it is suggested over no treatment for maintaining remission
    - Methotrexate monotherapy is suggested against use for induction, as well as maintenance of remission
  - The combination of TNF-alpha antagonists (vedolizumab or ustekinumab) is suggested with thiopurines or methotrexate over biologic monotherapy or thiopurine monotherapy
  - Early use of biologics with or without immunomodulator therapy is suggested rather than gradual step up to these agents following failure of 5-ASA
  - Additional recommendations for adult outpatients with moderate to severe UC are provided regarding the use of tofacitinib and management of non-responders to infliximab
- For patients who achieve remission with biologic agents and/or immunomodulators or tofacitinib, it is suggested against continuing 5-ASA for induction and maintenance of remission

Treatment Guidelines

American Gastroenterology Association (AGA), 2021

- AGA published guidelines for the management of moderate to severe luminal and fistulizing Crohn's disease in adult outpatients
  - They recommend anti-TNFα therapy over no treatment for induction and maintenance of remission
  - Ustekinumab is recommended and vedolizumab is suggested over no treatment
  - They recommend against natalizumab over no treatment for induction and maintenance
  - Infliximab, adalimumab, or ustekinumab are recommended over certolizumab pegol and vedolizumab is suggested over certolizumab pegol for induction in patients naive to biologics

Cytokine & CAM Antagonist

- ustekinumab (Stelara)
  - **July 2020: FDA approved expanded indication for patients with moderate to severe plaque psoriasis who are ≥ 6 years old; previously, it was indicated only in patients ≥ 12 years old**
  - **Indications:**
    - Adult patients with: moderate to severe plaque psoriasis (Ps) who are candidates for phototherapy or systemic therapy; active psoriatic arthritis (PsA), alone or in combination with methotrexate; moderately to severely active Crohn's disease (CD); moderately to severely active ulcerative colitis
    - **Pediatric patients 6 years and older with moderate to severe plaque psoriasis, who are candidates for phototherapy or systemic therapy**
  - **Limitations**
    - Live vaccines should not be given with Stelara
    - Infections: Serious infections have occurred
      - Instruct patients to seek medical advice if signs or symptoms of clinically important chronic or acute infection occur
      - If a serious infection develops, discontinue until the infection resolves
    - May increase risk of malignancy
  - **Dosage**
    - Dosing stratified by indication - found in TCR and PI
  - **Availability**
    - Subcutaneous Injection: 45 mg/0.5 mL or 90 mg/mL solution in a single-dose prefilled syringe; 45 mg/0.5 mL solution in a single-dose vial
    - Intravenous Infusion: 130 mg/26 mL (5 mg/mL) solution in a single-dose vial

Cytokine & CAM Antagonist

- adalimumab-fkjp (Hulio)
  - **July 2020: FDA approved Hulio, a biosimilar to Humira; it is a TNF antagonist approved for the treatment of adults with moderately to severely active RA, JIA in patients ≥ 4 years of age, PsA in adults, active AS in adults, moderately to severely active UC, moderately to severely active CD, and moderate to severe plaque psoriasis**
  - **Indications:**
    - **Adults with moderately to severely active RA, JIA in patients ≥ 4 years of age, PsA in adults, active AS in adults, moderately to severely active UC, moderately to severely active CD, and moderate to severe plaque psoriasis**
  - **Limitations**
    - **BBW: Increased risk of serious infections leading to hospitalization or death, including tuberculosis (TB), bacterial sepsis, invasive fungal infections (such as histoplasmosis), and infections due to other opportunistic pathogens**
    - **BBW: Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers including adalimumab products**
    - **Serious infections: Do not start Hulio during an active infection. If an infection develops, monitor carefully, and stop if infection becomes serious**
  - **Dosage**
    - **Dosing stratified by indication - found in TCR and PI**
  - **Availability**
    - **Injection: 40 mg/0.8 mL in a single-dose prefilled pen (Hulio Pen)**
    - **Injection: 40 mg/0.8 mL in a single-dose prefilled plastic syringe**
    - **Injection: 20 mg/0.4 mL in a single-dose prefilled plastic syringe**

Cytokine & CAM Antagonist

- guselkumab (Tremfya)
  - **July 2020: FDA approved new indication for psoriatic arthritis**
  - **Indications:**
    - Treatment of adult patients with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy; **active psoriatic arthritis**
  - **Limitations**
    - Live vaccines should not be given with Tremfya
    - Infections: May increase the risk of infection
      - Instruct patients to seek medical advice if signs or symptoms of clinically important chronic or acute infection occur
      - If a serious infection develops, discontinue Tremfya until the infection resolves
    - Tuberculosis (TB): Evaluate for TB prior to initiating treatment
    - Safety and efficacy for patients < 18 years of age have not been established
    - There are no available data on Tremfya use in pregnant women to inform a drug associated risk of adverse developmental outcomes
    - No specific studies have been conducted to determine the effect of renal or hepatic impairment on the PK of Tremfya
  - **Dosage**
    - Plaque Psoriasis and **Active Psoriatic Arthritis:** 100 mg administered by subcutaneous injection at Week 0, Week 4 and every 8 weeks thereafter
  - **Availability**
    - Injection: 100 mg/mL in a single-dose prefilled syringe or single-dose OnePress patient-controlled injector

Cytokine & CAM Antagonist

- canakinumab (Ilaris)
  - **September 2020: FDA approved Ilaris for active Still's disease, including adult-onset Still's disease (AOSD) and systemic juvenile idiopathic arthritis (SJIA) in patients aged ≥ 2 years**
  - **Indications:**
    - Periodic Fever Syndromes: Cryopyrin-Associated Periodic Syndromes (CAPS), in adults and children 4 years of age and older, including: Familial Cold Auto-inflammatory Syndrome (FCAS); Muckle-Wells Syndrome (MWS)
    - Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS) in adult and pediatric patients
    - Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD) in adult and pediatric patients
    - Familial Mediterranean Fever (FMF) in adult and pediatric patients
    - **Active Still's disease, including Adult-Onset Still's Disease (AOSD) and Systemic Juvenile Idiopathic Arthritis (SJIA) in patients aged 2 years and older**
  - **Limitations**
    - Live vaccines should not be given with Ilaris
    - Infections: Serious infections have occurred
      - Instruct patients to seek medical advice if signs or symptoms of clinically important chronic or acute infection occur
      - If a serious infection develops, discontinue until the infection resolves
    - CAPS: The most common adverse reactions greater than 10% reported by patients treated with ILARIS are nasopharyngitis, diarrhea, influenza, rhinitis, nausea, headache, bronchitis, gastroenteritis, pharyngitis, weight increased, musculoskeletal pain, and vertigo
  - **Dosage**
    - Dosing stratified by indication - found in TCR and PI
  - **Availability**
    - Injection: 150 mg/mL solution in single-dose vials

Cytokine & CAM Antagonist

- satralizumab-mwge (Enspryng)
  - **August 2020: FDA approved Enspryng, an interleukin-6 (IL-6) receptor antagonist for the treatment of neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive**
  - **Indications:**
    - **Treatment of neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive**
  - **Limitations**
    - **Infections: Delay administration in patients with an active infection until the infection is resolved. Vaccination with live or live-attenuated vaccines is not recommended during treatment**
    - **Elevated Liver Enzymes: Monitor ALT and AST levels during treatment; interruption of treatment may be required**
    - **Decreased Neutrophil Counts: Monitor neutrophils during treatment**
  - **Dosage**
    - **Hepatitis B virus, tuberculosis, and liver transaminase screening is required before the first dose**
    - **Prior to every use, determine if there is an active infection**
    - **The recommended loading dosage for the first three administrations is 120 mg by subcutaneous injection at Weeks 0, 2, and 4, followed by a maintenance dosage of 120 mg every 4 weeks**
  - **Availability**
    - **Injection: 120 mg/mL in a single-dose prefilled syringe**

Cytokine & CAM Antagonist

- tofacitinib (Xeljanz and Xeljanz XR)
  - **September 2020: FDA approved Xeljanz 1 mg/mL oral solution and Xeljanz tablets for the treatment of polyarticular course juvenile idiopathic arthritis (pcJIA) in patients ≥ 2 years old**
  - **Indication**
    - Rheumatoid Arthritis (RA), Psoriatic Arthritis (PsA), Ulcerative Colitis (UC), and **Polyarticular Course Juvenile Idiopathic Arthritis**
  - **Limitations**
    - Warnings:
      - Boxed warnings include increased risk of serious and sometimes fatal bacterial, mycobacterial, fungal, and viral infections in patients treated with tofacitinib
      - Thrombosis, including pulmonary embolism, deep venous thrombosis and arterial thrombosis have occurred in patients treated with Xeljanz and other Janus kinase inhibitors. Rheumatoid arthritis patients with at least one cardiovascular (CV) risk factor had a higher rate of all-cause mortality and thrombosis with Xeljanz 10 mg twice daily vs. 5 mg twice daily or TNF blockers
      - Lymphoma and other malignancies have been observed in patients treated with Xeljanz, including an increased rate of Epstein Barr Virus-associated post-transplant lymphoproliferative disorder
  - **Dosage**
    - **Dosing stratified by indication - found in TCR**
  - **Availability**
    - Tablets: 5 mg, 10 mg
    - XR Tablets: 11 mg, 22 mg
    - **Oral Solution: 1 mg/mL**

Cytokine & CAM Antagonist

- golimumab (Simponi Aria)
  - **October 2020: FDA approved Simponi Aria for the treatment of active polyarticular juvenile idiopathic arthritis (pJIA) in patients ≥ 2 years old**
  - **October 2020: FDA also expanded indication for use in PsA to include children as young as 2 years old (previously, it was approved for use only in adults)**

  - **Indication**
    - **Active Psoriatic Arthritis (PsA) in patients 2 years of age and older**
    - **Active polyarticular Juvenile Idiopathic Arthritis (pJIA) in patients 2 years of age and older**
    - Adult patients with moderately to severely active Rheumatoid Arthritis (RA) in combination with methotrexate
    - Adult patients with active Ankylosing Spondylitis (AS)
  - **Limitations**
    - Warnings:
      - Boxed warnings include increased risk of serious and sometimes fatal bacterial, mycobacterial, fungal, and viral infections
      - Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers
  - **Dosage**
    - **Dosing stratified by indication - found in TCR**
  - **Availability**
    - Injection: 50 mg/4 mL (12.5 mg/mL) solution in a single-dose vial

Cytokine & CAM Antagonist

- anakinra (Kineret)
  - **December 2020: FDA also expanded indication for use in the treatment of Deficiency of Interleukin-1 Receptor Antagonist (DIRA)**
  - **Indication**
    - Rheumatoid Arthritis (RA): Reduction in signs and symptoms and slowing the progression of structural damage in moderately to severely active rheumatoid arthritis, in patients 18 years of age or older who have failed 1 or more disease modifying antirheumatic drugs (DMARDs)
    - Cryopyrin-Associated Periodic Syndromes (CAPS): Treatment of Neonatal-Onset Multisystem Inflammatory Disease (NOMID)
    - **Deficiency of Interleukin-1 Receptor Antagonist (DIRA): Treatment of Deficiency of Interleukin-1 Receptor Antagonist (DIRA)**
  - **Warnings**
    - In RA, discontinue use if serious infection develops. In Kineret treated NOMID or DIRA patients, the risk of a disease flare when discontinuing KINERET treatment should be weighed against the potential risk of continued treatment. Do not initiate Kineret in patients with active infections
    - The impact of treatment with Kineret on active and/or chronic infections and the development of malignancies is not known
    - Live vaccines should not be given concurrently with Kineret
    - Neutrophil counts should be assessed prior to initiating Kineret treatment, and while receiving Kineret, monthly for 3 months, and thereafter quarterly for a period up to 1 year
  - **Dosage**
    - **Dosing stratified by indication - found in TCR**
  - **Availability**
    - Injection: 100 mg/0.67 mL solution in a single-use prefilled syringe for subcutaneous injection. Graduated syringe allows for doses between 20 mg and 100 mg

Cytokine & CAM Antagonist

- rilonacept (Arcalyst)
  - **December 2020: FDA expanded indication for use in the treatment of Deficiency of Interleukin-1 Receptor Antagonist (DIRA)**
  - **March 2021: FDA expanded indication for use in treatment of recurrent pericarditis (RP) and reduction in risk of recurrence in adults and children ≥ 12 years old**
  - **Indication**
    - Treatment of Cryopyrin-Associated Periodic Syndromes (CAPS), including Familial Cold Auto-inflammatory Syndrome (FCAS), and Muckle-Wells Syndrome (MWS) in adults and children 12 years and older
    - **Maintenance of remission of Deficiency of Interleukin-1 Receptor Antagonist (DIRA) in adults and pediatric patients weighing 10 kg or more**
    - **Treatment of recurrent pericarditis (RP) and reduction in risk of recurrence in adults and children 12 years and older**
  - **Warnings**
    - Serious Infections: Serious, life-threatening infections have been reported in patients taking ARCALYST. Do not initiate treatment with ARCALYST in patients with active or chronic infections. Discontinue treatment if a patient develops a serious infection
    - Hypersensitivity Reactions: If a hypersensitivity reaction occurs, discontinue administration of ARCALYST and initiate appropriate therapy
    - Immunizations: Avoid live vaccines. Update recommended vaccinations prior to initiation of therapy per current guidelines
  - **Dosage**
    - **Dosing stratified by indication - found in TCR**
  - **Availability**
    - For injection: 220 mg of lyophilized powder in a single-dose vial for reconstitution

Cytokine & CAM Antagonist

- adalimumab (Humira)
  - **February 2021: FDA expanded the indication for treatment of moderately to severely active UC to include patients as young as 5 years old**
  - **Indication**
    - Rheumatoid Arthritis (RA), Juvenile Idiopathic Arthritis (JIA), Psoriatic Arthritis (PsA), Ankylosing Spondylitis (AS), Crohn's Disease (CD), **Ulcerative Colitis (UC)**, Plaque Psoriasis (Ps), Hidradenitis Suppurativa (HS), Uveitis (UV)
  - **Warnings**
    - Serious Infections: Serious, life-threatening infections have been reported in patients taking ARCALYST. Do not initiate treatment with ARCALYST in patients with active or chronic infections. Discontinue treatment if a patient develops a serious infection
    - Hypersensitivity Reactions: If a hypersensitivity reaction occurs, discontinue administration of ARCALYST and initiate appropriate therapy
    - Immunizations: Avoid live vaccines. Update recommended vaccinations prior to initiation of therapy per current guidelines
  - **Dosage**
    - **Dosing stratified by indication, age and weight - found in TCR**
  - **Availability**
    - Injection: Single-dose prefilled pen (HUMIRA Pen): 80 mg/0.8 mL, 40 mg/0.8 mL, and 40 mg/0.4 mL
    - Single-dose prefilled glass syringe: 80 mg/0.8 mL, 40 mg/0.8 mL, 40 mg/0.4 mL, 20 mg/0.4 mL, 20 mg/0.2 mL, 10 mg/0.2 mL, 10 mg/0.1 mL
    - Single-dose glass vial for institutional use only: 40 mg/0.8 mL

Cytokine & CAM Antagonist

- tocilizumab (Actemra)
  - **March 2021: FDA issued EUA for tocilizumab, an IL-6 blocking monoclonal antibody, for the treatment of hospitalized adults and pediatric patients ≥ 2 years old for COVID-19 who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO). Tocilizumab is already approved for the treatment of select pts with RA, interstitial lung disease, giant cell arteritis, and JIA**
  - **Indication**
    - Rheumatoid Arthritis (RA), Giant Cell Arteritis (GCA), Systemic Sclerosis-Associated Interstitial Lung Disease, Polyarticular Juvenile Idiopathic Arthritis (PJIA), Systemic Juvenile Idiopathic Arthritis (SJIA), Cytokine Release Syndrome (CRS)
  - **Warnings**
    - Serious Infections – do not administer during an active infection, including localized infections. If a serious infection develops, interrupt treatment until the infection is controlled
    - Hepatotoxicity- Monitor patients for signs and symptoms of hepatic injury. Modify or discontinue if abnormal liver tests persist or worsen or if clinical signs and symptoms of liver disease develop
    - Immunizations: Avoid live vaccines
  - **Dosage**
    - **Dosing stratified by indication, age and weight - found in TCR**
  - **Availability**
    - Intravenous Infusion: 80 mg/4 mL (20 mg/mL), 200 mg/10 mL (20 mg/mL), 400 mg/20 mL (20 mg/mL) in single-dose vials for further dilution prior to intravenous infusion
    - Subcutaneous Injection: 162 mg/0.9 mL in a single-dose prefilled syringe or single-dose prefilled ACTPen® autoinjector

Cytokine & CAM Antagonist

- secukinumab (Cosentyx)
  - **June 2021: FDA has expanded the use for moderate to severe plaque psoriasis in patients who are candidates for systemic therapy or phototherapy to include patients ≥ 6 years; previously this indication was only approved for use in adults**
  - **Indication**
    - **Moderate to severe plaque psoriasis in patients 6 years and older who are candidates for systemic therapy or phototherapy**
    - Adults with active psoriatic arthritis (PsA)
    - Adults with active ankylosing spondylitis (AS)
    - Adults with active non-radiographic axial spondyloarthritis (nr-axSpA) with objective signs of inflammation
  - **Warnings**
    - Infections: Serious infections have occurred. Caution should be exercised when considering the use of Cosentyx in patients with a chronic infection or a history of recurrent infection. If a serious infection develops, discontinue Cosentyx until the infection resolves
    - Tuberculosis (TB): Prior to initiating treatment with Cosentyx, evaluate for TB
    - Inflammatory Bowel Disease: Cases of inflammatory bowel disease were observed in clinical trials. Caution should be exercised when prescribing Cosentyx to patients with inflammatory bowel disease
    - Immunizations: Avoid live vaccines
  - **Dosage**
    - **Dosing stratified by indication, age and weight - found in TCR**
  - **Availability**
    - Injection: 150 mg/mL solution in a single-dose Sensoready pen and in a single-dose prefilled syringe
    - Injection: 75 mg/0.5 mL solution in a single-dose prefilled syringe (for pediatric patients)
    - For Injection: 150 mg, lyophilized powder in a single-dose vial for reconstitution (for healthcare professional use only)

Cytokine & CAM Antagonist

- Discontinuation
  - **adalimumab (Humira) – July 2020**
    - **Abbvie reported to FDA plans to DC the 10 mg/0.2 mL (NDC 0074-6347-02) and 20 mg/0.4 mL (NDC 0074-9374-02) pre-filled syringe presentations based on market assessment and product demand**

- FDA Communication
  - **tofacitinib (Xeljanz, Xeljanz XR) – February 2021**
    - **FDA is alerting the public that preliminary results from a safety clinical trial show an increased risk of serious heart-related problems and cancer with tofacitinib compared to TNF inhibitors**
    - **FDA advises patients should not stop taking prescribed tofacitinib without consulting their physician**
    - **FDA will communicate final conclusions and recommendations once their review is complete**

- REMS Update
  - **brodalumab (Siliq) – February 2021**
    - **Various updates to the REMS material including conversion of the REMS Document to a new format and removal of the "program" from the titles of the REMS materials**
    - **Additionally, changes were made to the Stakeholder Enrollment Form and Patient Enrollment Form as well as to the REMS materials to align with changes to the REMS Document**

Magellan Rx MANAGEMENT℠

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Movement Disorder Agents

Movement Disorders – Disease State Description/Guidelines

Huntington's Disease (HD)

- Chorea, an abnormal involuntary twisting or writhing movement, is a characteristic feature of Huntington's disease (HD), a rare and fatal genetic disorder resulting in neurodegeneration of the brain, which affects over 35,000 people in the United States (US)
  - As chorea becomes more severe, it can interfere with patients' function. As the disease progresses, chorea is replaced by dystonia and parkinsonism
  - Chorea affects approximately 90% of people with HD. It often develops early, gradually worsens, and plateaus in late stages. Chorea symptoms may be aggravated by stress and anxiety
- No therapy currently exists to delay the onset of symptoms or prevent the progression of the disease; however, symptomatic treatment may improve the quality of life and prevent complications
  - Tetrabenazine (Xenazine), a vesicular monoamine transporter 2 (VMAT2) inhibitor, was the first agent approved (2008) by the Food and Drug Administration (FDA) to treat chorea associated with HD
  - A deuterated formulation allowing once-daily dosing, deutetrabenazine (Austedo), was approved to treat chorea associated with HD in 2017
  - Other therapeutic options that are used but lack FDA approval for this use (off-label) include dopamine-depleting agents (e.g., reserpine) and dopamine-receptor antagonists (neuroleptics). However, long-term use of these drugs may carry a high risk of adverse effects

- **American Academy of Neurology (AAN), 2012**
  - Recommend tetrabenazine (up to 100 mg per day), amantadine, or riluzole for chorea associated with HD
  - Guidelines state that neuroleptics may be reasonable options given the behavioral concerns; reserpine and deutetrabenazine are not addressed in the AAN guidelines
  - Guidelines advise that the decision by physicians and patients whether chorea requires pharmacologic treatment should consider matters such as mood disturbance, cognitive decline, drug adverse effects, and polypharmacy risks
  - These guidelines were reaffirmed in 2015, but an update is in progress

Movement Disorders – Disease State Description/Guidelines

- **Tardive dyskinesia (TD)**
  - Consists of involuntary movements of the tongue, lips, face, trunk, and extremities that occur in patients treated with medications with dopamine antagonist properties
  - It may consist of movements classified as bradykinesia and/or hyperkinesia. Dopamine transporter dysfunction and chronic central dopamine blockade have been hypothesized to play a role in the development of TD, although multiple other pathophysiologic mechanisms have been proposed
  - TD differs from acute movement disorders, often referred to as extrapyramidal symptoms (EPS), which commonly occur in patients treated with dopamine antagonists. EPS most commonly occurs early in therapy and during dose increases
  - These acute movement disorders include akathisia, acute dystonia, parkinsonism, and other hyperkinetic dyskinesias. TD generally occurs after long-term treatment with a dopamine antagonizing medication, but the timeline of TD onset varies extensively. Once a patient develops TD, it may be irreversible

Movement Disorders

- valbenazine (Ingrezza)
  - **April 2021: FDA has expanded formulation to include 60 mg capsule strengths**
  - **Indication**
    - Treatment of adults with tardive dyskinesia
  - **Warnings**
    - Somnolence: May impair patient's ability to drive or operate hazardous machinery
    - QT Prolongation: May cause an increase in QT interval. Avoid use in patients with congenital long QT syndrome or with arrhythmias associated with a prolonged QT interval
    - Pregnancy: May cause fetal harm
    - Lactation: Advise not to breastfeed
  - **Dosage**
    - The initial dosage is 40 mg once daily. After one week, increase the dose to the recommended dosage of 80 mg once daily
    - The recommended dosage for patients with moderate or severe hepatic impairment is 40 mg once daily
  - **Availability**
    - **Capsules:** 40 mg, **60 mg**, and 80 mg

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Ophthalmic Agents: Glaucoma Agents

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

- 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

Ophthalmic, Glaucoma Agents – Guidelines

- **Discontinuation**
  - echothiophate iodide, 0.125% (Phospholine Iodide) – October 2020
    - **The FDA has announced the discontinuation of Phospholine Iodide, 6.25 mg package**
    - **Pfizer, expects product will remain available through May 1, 2021**

- **Generic**
  - brinzolamide – December 2020
    - **FDA approved first generic for Novartis' Azopt**

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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 tear deficiency) or rapid evaporative loss (evaporative tear deficiency) 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

- loteprednol etabonate ophthalmic suspension, 0.25% (Eysuvis)
  - **October 2020: FDA approved Eysuvis, a corticosteroid indicated for the short-term (up to 2 two weeks) treatment of the signs and symptoms of dry eye disease**
  - **Indication**
    - **The short-term (up to two weeks) treatment of the signs and symptoms of dry eye disease**
  - **Warning/Precautions**
    - **Contraindicated in most viral diseases of the cornea and conjunctiva including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, and varicella, and also in mycobacterial infection of the eye and fungal diseases of ocular structures**
    - **Delayed Healing and Corneal Perforation: The initial prescription and each renewal of the medication order should be made by a physician only after examination of the patient with the aid of magnification, such as slit lamp biomicroscopy, and, where appropriate, fluorescein staining**
    - **Intraocular Pressure (IOP) Increase: Prolonged use of corticosteroids may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision. Renewal of the medication order should be made by a physician only after examination of the patient and evaluation of the IOP**
  - **Dosage**
    - **Shake for two to three seconds before using**
    - **Instill one to two drops into each eye four times daily**
  - **Availability**
    - **Ophthalmic suspension containing 2.5 mg/mL of loteprednol etabonate**

Ophthalmic Agents – Immunomodulators

- cyclosporine (Verkazia)
  - **June 2021: FDA approved Verkazia, a calcineurin inhibitor immunosuppressant, for the treatment of vernal keratoconjunctivitis (VKC) in children and adults**
  - **Indication**
    - **Treatment of vernal keratoconjunctivitis in children and adults**
  - **Warning/Precautions**
    - **To avoid the potential for eye injury and contamination, advise patient not to touch the vial tip to the eye or other surfaces**
  - **Dosage**
    - **Instill one drop of Verkazia, 4 times daily (morning, noon, afternoon, and evening) in each affected eye**
  - **Availability**
    - **Ophthalmic emulsion: 0.1% (1 mg/mL) cyclosporine**

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Respiratory Agents: Pulmonary Fibrosing Agents

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Smoking Deterrents

Smoking Cessation Agents - Disease State Description/Guidelines

- Cigarette smoking is the leading preventable cause of death and is responsible for about 1 in 5 deaths annually, or about 480,000 deaths per year in the United States
- Approximately 70% of smokers have a desire to quit completely, and 55% have made a quit attempt in the past year
  - Discontinuing smoking often requires multiple attempts
  - Most attempts are unsuccessful because they are unaided
  - Relapse is often caused by stress, weight gain, and withdrawal symptoms
    - Examples of common nicotine withdrawal symptoms include irritability, anxiety, difficulty concentrating, and increased appetite

CDC, 2018

- American Thoracic Society (ATS), 2020
  - ATS published new clinical practice guidelines on initiation of pharmacotherapy for tobacco dependence in adults
  - The guidance maintains all patients who are using tobacco should receive treatment for dependence, and not only be encouraged to discontinue tobacco use
  - Strong recommendations include:
    - 1) Preference for use of varenicline over a nicotine patch
    - 2) Preference for varenicline over bupropion
    - 3) Use of varenicline rather than a nicotine patch in adults with comorbid psychiatric condition(s)
    - 4) Starting varenicline in adults even if they are not ready to quit
    - 5) Using controller therapy for an extended duration of more than 12 weeks
  - Conditional recommendations include:
    - 1) The combination of a nicotine patch with varenicline overuse of varenicline alone
    - 2) Use of varenicline over electronic cigarettes

Smoking Cessation Agents - Disease State Description/Guidelines

- US Preventative Services Task Force (USPSTF), 2021
  - Recommended that clinicians ask all adults, about tobacco use and to advise current users to stop using tobacco, and provide behavioral interventions, including approved pharmacotherapy for tobacco use cessation (Level A recommendation)
  - Clinicians should also advise pregnant women to stop using tobacco and provide behavioral interventions; however, evidence is not sufficient to assess benefits versus risks of pharmacotherapy use in pregnant women
  - In April 2020, the USPSTF issued a recommendation for school-aged children and adolescents who have not started to use tobacco stating that primary care clinicians are recommended to provide interventions (e.g., education or brief counseling), in order to prevent tobacco use initiation in these individuals (Level B recommendation)
  - However, for school-aged children and adolescents who use tobacco, it was concluded the current evidence is inadequate to determine the benefits versus risks of primary care-feasible interventions regarding tobacco cessation (Level I [insufficient] recommendation)

Magellan Rx MANAGEMENT

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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 191,930 cases projected to be diagnosed in 2020
- While prostate cancer accounts for the largest percentage of diagnosed cases in US males (20%), it only accounts for about 10% of all cancer deaths in this population, far behind lung cancer, the leading cause of cancer death, which accounts for 24% 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 9 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
- Additionally, the use of oral poly (ADP-ribose) polymerase (PARP) inhibitors in select prostate cancer patients is included in a separate Therapeutic Class Review
- The use of docetaxel, cabazitaxel, sipuleucel-T, pembrolizumab and radium-223 for the management of metastatic prostate cancer is beyond the scope of this review and will not be discussed in detail in this review

Oncology, Oral- Prostate

- enzalutamide (Xtandi)
  - **August 2020: FDA approved a new tablet formulation of Xtandi in 40 mg and 80 mg strengths. Like the previously approved 40 mg capsule, it is approved for the treatment of patients with castration-resistant prostate cancer and metastatic castration-sensitive prostate cancer**
  - **Indications**
    - **Castration-resistant prostate cancer**
    - **Metastatic castration-sensitive prostate cancer**
  - **Warning/Precautions**
    - Ischemic Heart Disease: Optimize management of cardiovascular risk factors. Discontinue XTANDI for Grade 3-4 events
    - Falls and Fractures occurred in 11% and 10% of patients receiving Xtandi, respectively. Evaluate patients for fracture and fall risk, and treat patients with bone-targeted agents according to established guidelines
    - Embryo-Fetal Toxicity: Can cause fetal harm and loss of pregnancy. Advise males with female partners of reproductive potential to use effective contraception
  - **Dosage**
    - 160 mg (two 80 mg tablets or four 40 mg tablets or four 40 mg capsules) administered orally once daily
    - Patients receiving Xtandi should also receive a gonadotropin-releasing hormone (GnRH) analog concurrently or should have had bilateral orchiectomy
  - **Availability**
    - Capsule 40 mg
    - **Tablet: 40 mg, 80 mg**

Oncology, Oral- Prostate

- relugolix (Orgovyx)
  - **December 2020: FDA approved relugolix (Orgovyx), a gonadotropin-releasing hormone (GnRH) receptor antagonist, indicated for the treatment of adult patients with advanced prostate cancer**
  - **Indications**
    - **Treatment of adult patients with advanced prostate cancer**
  - **Warning/Precautions**
    - **QT/QTc Interval Prolongation: Androgen deprivation therapy may prolong the QT interval**
    - **Embryo-Fetal Toxicity: Can cause fetal harm and loss of pregnancy. Advise males with female partners of reproductive potential to use effective contraception**
  - **Dosage**
    - **A loading dose of 360 mg on the first day of treatment followed by 120 mg taken orally once daily, at approximately the same time each day**
  - **Availability**
    - **Tablets: 120 mg**

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Oncology, Oral - Hematologic

Oncology, Oral- Hematological – Overview of Disease State

- **Marginal Zone Lymphoma (MZL)**
  - MZLs account for approximately 10% of all NHLs and are generally divided into 3 subtypes, nodal MZL, splenic MZL, and the most common subtype, mucosa-associated lymphoid tissue (MALT lymphoma)
  - Lenalidomide plus rituximab is an NCCN category 2B recommendation for first-line therapy of MZLs
  - For elderly or infirm patients, chlorambucil with or without rituximab may also be utilized in the first-line setting
  - Both lenalidomide with or without rituximab and ibrutinib as a single agent are NCCN V4.2020 category 2A, preferred recommendations for second- and subsequent-line therapy of MZL
  - Idelalisib or duvelisib may be used in the second- and subsequent-line of marginal zone lymphoma in patients who are relapsed/refractory after 2 prior therapies
- **Acute Myeloid Leukemia (AML)**
  - Most common form of acute leukemia among adults estimated 5,930 cases diagnosed and 1,500 deaths in the US in 2019
  - In patients who obtain a CR, 3 year survival is 45%, remission rates are inversely proportional to age
  - Cytogenetics plays a large role in determining prognosis and treatment options
  - Acute Promyelocytic Leukemia (APL) is a subtype of AML with distinct features and treatment
- **Diffuse Large B cell lymphoma (DLBCL)**
  - DLBCLs are the most common type of lymphoma and account for 30% of all NHL
  - There are several subtypes of DLBCL, including DLBCL arising from follicular lymphoma (FL)
  - Some patients with FL may undergo conversion to more aggressive lymphomas, such as DLBCL, and this risk increases over time; about 30% of FL patients convert to a more aggressive lymphoma at 10 years post-FL diagnosis
  - The B-cell lymphoma NCCN guidelines V4.2020 list selinexor (Xpovio) as an option for DLBCL not otherwise specified, including DLBCL arising from FL after at least 2 prior systemic therapies

Oncology, Oral- Hematological – Overview of Disease State

- **Kaposi Sarcoma**
  - Kaposi sarcoma (KS) is a malignancy of the endothelial cells and is characterized by cutaneous red or brown papules, often seen on the lower extremities
  - There are 4 types of KS. Classic KS presents with cutaneous lesions but follows an indolent course
  - It is most common in elderly patients of Mediterranean, Eastern European, Middle Eastern, and/or Jewish descent
  - Endemic KS tends to be more aggressive than classic KS and occurs in younger patients (< 40 years old), as well as in children in equatorial Africa
  - The third type of KS is iatrogenic and occurs in the setting of patients taking immunosuppressive therapy (e.g., organ transplant recipients)
  - The fourth type of KS is seen in patients infected with the human immunodeficiency virus (HIV). In these patients, KS is considered to be an acquired immune deficiency syndrome (AIDS)-defining cancer
  - The risk for developing KS is estimated to be approximately 498-fold higher in HIV-positive patients compared to the general United Stated (US) population
  - Due to the improved treatment options available to AIDS patients, the incidence of this cancer has been declining.
  - The NCCN V3.2020 guidelines for AIDS-related KS list pomalidomide (Pomalyst) as a preferred systemic therapy option for patients with relapsed/refractory disease and note that pomalidomide has been FDA approved for the treatment of adult patients with AIDS-related KS after failure of highly active antiretroviral therapy

Oncology, Oral- Hematological – Guidelines

- **American Society of Hematology, 2020**
  - Published guidelines for the treatment of newly diagnosed AML in older adults
  - This guideline examined questions around the role of treatment for older adults with AML and the intensity and length of treatment in this patient population
  - The general conclusion of the panel of experts was that for older adults, treatment is recommended over best supportive care, and more-intensive therapy is recommended over less-intensive therapy when it is tolerable to the patient
  - Specific recommendations pertaining to patients who are not appropriate for intensive antileukemic therapy but who are able to receive treatment include a recommendation of monotherapy (e.g., glasdegib, venetoclax) over combination therapy (conditional recommendation based on low certainty)
  - The guidelines further note that when these patients choose combination therapy, there is evidence to support the use LDAC in combination with venetoclax

Oncology, Oral- Hematological - Overview of Disease State

- ONCOLOGY AGENTS : ANTINEOPLASTICS - MISC COMBINATIONS – ORAL
  - **Inqovi**
- ONCOLOGY AGENTS : HEDGEHOG PATHWAY INHIBITORS – ORAL
  - Daurismo
- ONCOLOGY AGENTS : MULTIKINASE INHIBITORS – ORAL
  - Rydapt
  - **Ukoniq**
- ONCOLOGY AGENTS : TYROSINE KINASE INHIBITORS – ORAL
  - Bosulif
  - Brukinsa
  - Gleevec
  - **Iclusig**
  - Imatinib
  - Imbruvica
  - Sprycel
  - Tasigna
  - Xospata
- ONCOLOGY AGENTS : RETINOIDS – ORAL
  - Tretinoin

Oncology, Oral- Hematological

- decitabine/cedazuridine (Inqovi)
  - August 2020: FDA approved Inqovi, a combination of decitabine (a nucleoside metabolic inhibitor) and cedazuridine (a cytidine deaminase inhibitor) indicated for treatment of adult patients with myelodysplastic syndromes (MDS), including previously treated and untreated, de novo and secondary MDS with the following French American-British subtypes (refractory anemia, refractory anemia with ringed sideroblasts, refractory anemia with excess blasts, and chronic myelomonocytic leukemia [CMML]) and intermediate-1, intermediate-2, and high-risk International Prognostic Scoring System groups
  - Indication
    - A combination of decitabine, a nucleoside metabolic inhibitor, and cedazuridine, a cytidine deaminase inhibitor, indicated for treatment of adult patients with myelodysplastic syndromes (MDS), including previously treated and untreated, de novo and secondary MDS with the following FrenchAmerican-British subtypes (refractory anemia, refractory anemia with ringed sideroblasts, refractory anemia with excess blasts, and chronic myelomonocytic leukemia [CMML]) and intermediate-1, intermediate-2, and high-risk International Prognostic Scoring System groups
  - Warnings and Precautions
    - Myelosuppression: Fatal and serious myelosuppression and infectious complications can occur. Obtain complete blood cell counts prior to initiation of treatment, prior to each cycle, and as clinically indicated to monitor for response and toxicity. Delay the next cycle and resume at the same or reduced dose as recommended
    - Embryo-Fetal Toxicity: Can cause fetal harm. Advise patients of the potential risk to a fetus and use of effective contraception
    - Drugs Metabolized by Cytidine Deaminase: Avoid coadministration with Inqovi
  - Dosage
    - The recommended dosage of INQOVI is 1 tablet (35 mg decitabine and 100 mg cedazuridine) taken orally once daily on Days 1 through 5 of each 28-day cycle
  - Availability
    - Tablets: 35 mg decitabine and 100 mg cedazuridine

Oncology, Oral- Hematological

- ponatinib (Iclusig)
  - **December 2020: The FDA approved a new indication for the treatment of adults with: chronic phase (CP) chronic myeloid leukemia (CML) with resistance or intolerance to ≥ 2 prior kinase inhibitors**
  - **Indication**
    - **Chronic phase (CP) chronic myeloid leukemia (CML) with resistance or intolerance to at least two prior kinase inhibitors**
    - Accelerated phase (AP) or blast phase (BP) CML or Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL) for whom no other kinase inhibitors are indicated
    - T315I-positive CML (chronic phase, accelerated phase, or blast phase) or T315I-positive Ph+ ALL
    - Limitations of Use: Iclusig is not indicated and is not recommended for the treatment of patients with newly diagnosed CP-CML
  - **Warnings and Precautions**
    - BBW: VTEs, Heart Failure, Hepatotoxicity, and Arterial Occlusive Events.
    - Tumor Lysis Syndrome: Ensure adequate hydration and correct elevated uric acid levels prior to initiating Iclusig
    - Embryo-Fetal Toxicity: Can cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception
    - Lactation: Advise not to breastfeed
  - **Dosage**
    - **Recommended Dosage in CP-CML: Starting dose is 45 mg orally once daily with a reduction to 15 mg once daily upon achievement of ≤1% BCR-ABL1IS**
    - Recommended Dosage in AP-CML, BP-CML, and Ph+ ALL: Starting dose is 45 mg orally once daily
  - **Availability**
    - Tablets: 10 mg, 15 mg, 30 mg and 45 mg

Oncology, Oral- Hematological

- umbralisib (Ukoniq)
  - **February 2021: The FDA has granted Accelerated Approval to umbralisib (Ukoniq), a kinase inhibitor, for the treatment of adults with relapsed or refractory marginal zone lymphoma (MZL) who have received ≥ 1 prior anti-CD20-based regimen OR relapsed or refractory follicular lymphoma (FL) who have received ≥ 3 prior lines of systemic therapy**
  - **Indication**
    - **The treatment of adult patients with:**
      - **Relapsed or refractory marginal zone lymphoma (MZL) who have received at least one prior anti-CD20-based regimen**
      - **Relapsed or refractory follicular lymphoma (FL) who have received at least three prior lines of systemic therapy**
    - **These indications are approved under accelerated approval based on overall response rate. Continued approval for these indications may be contingent upon verification and description of clinical benefit in a confirmatory trial**
  - **Warnings and Precautions**
    - **Infections: Monitor for fever and any new or worsening signs and symptoms of infection. Evaluate promptly and treat as needed**
    - **Neutropenia: Monitor blood counts during treatment**
    - **Diarrhea or Non-infectious colitis: Monitor for the development of diarrhea or colitis and provide supportive care as appropriate**
    - **Hepatotoxicity: Monitor hepatic function**
  - **Dosage**
    - **Recommended dosage: 800 mg orally once daily with food**
    - **Manage toxicity using treatment interruption, dose reduction, or discontinuation**
  - **Availability**
    - **Tablets: 200 mg**

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Oncology, Oral - Breast

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 281,550 new cases of breast cancer diagnosed in the US in 2021 and there will be an estimated 43,600 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 41% since 1989, largely due to improvements in both early detection and treatment
  - The overall 5-year survival for women diagnosed with breast cancer is 90%
  - 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 28.1%
  - 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 – Guidelines

- **American Society of Hematology, 2020**
  - Published guidelines for the treatment of newly diagnosed AML in older adults
  - This guideline examined questions around the role of treatment for older adults with AML and the intensity and length of treatment in this patient population
  - The general conclusion of the panel of experts was that for older adults, treatment is recommended over best supportive care, and more-intensive therapy is recommended over less-intensive therapy when it is tolerable to the patient
  - Specific recommendations pertaining to patients who are not appropriate for intensive antileukemic therapy but who are able to receive treatment include a recommendation of monotherapy (e.g., glasdegib, venetoclax) over combination therapy (conditional recommendation based on low certainty)
  - The guidelines further note that when these patients choose combination therapy, there is evidence to support the use LDAC in combination with venetoclax

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
  - **Talzenna**

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

Oncology, Oral- Breast

- neratinib (Nerlynx)
  - **August 2020: FDA approved for use in combination with capecitabine, for the treatment of adult patients with advanced or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2 based regimens in the metastatic setting; already indicated as a single agent, for the extended adjuvant treatment of adult patients with early stage HER2-positive breast cancer, to follow adjuvant trastuzumab-based therapy**
  - **Indications**
    - As a single agent, for the extended adjuvant treatment of adult patients with early stage HER2-positive breast cancer, to follow adjuvant trastuzumab based therapy
    - **In combination with capecitabine, for the treatment of adult patients with advanced or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2 based regimens in the metastatic setting**
  - **Warnings and Precautions**
    - Diarrhea: Aggressively manage diarrhea. If diarrhea occurs despite recommended prophylaxis, treat with additional antidiarrheals, fluids, and electrolytes as clinically indicated. Withhold Nerlynx in patients experiencing severe and/or persistent diarrhea. Hepatotoxicity: Monitor liver function tests monthly for the first 3 months of treatment, then every 3 months while on treatment and as clinically indicated. Withhold Nerlynx in patients experiencing Grade 3 liver abnormalities and permanently discontinue Nerlynx in patients experiencing Grade 4 liver abnormalities
    - Embryo-Fetal Toxicity: Can cause fetal harm. Advise patients of the potential risk to a fetus and use of effective contraception
  - **Dosage**
    - **Stratified by indication (found in TCR or Package Insert)**
  - **Availability**
    - Tablets: 40 mg

Oncology, Oral- Breast

- talazoparib (Talzenna)
  - **October 2020: FDA approved use in patients with severe renal impairment (CrCl 15-29 mL/min)**
  - **Indications**
    - **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**
    - Myelodysplastic Syndrome/Acute Myeloid Leukemia (MDS/AML): MDS/AML has been reported in 2 out of 584 (0.3%) solid tumor patients treated with Talzenna in clinical studies. Monitor patients for hematological toxicity at baseline and monthly thereafter. Discontinue if MDS/AML is confirmed
    - Embryo-Fetal Toxicity: Can cause fetal harm. Advise patients of the potential risk to a fetus and use of effective contraception
  - **Dosage**
    - 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
    - P-gp Inhibitors: Reduce Talzenna dose for certain P-gp inhibitors, and monitor for potential increased adverse reactions as appropriate
  - **Availability**
    - Capsules: 0.25 mg, 1 mg

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Oncology, Oral – Renal Cell Carcinoma

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 64 years, and > 75% of cases are diagnosed in patients ages 55 or older
  - The overall 5-year survival for patients diagnosed with RCC was 75.6% from the period of 2011 to 2017
  - 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 14% 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

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- 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

- **axitinib (Inlyta)**
  - June 2020: 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
    - In combination with avelumab, for the first-line treatment of patients with advanced renal cell carcinoma (RCC)
    - In combination with pembrolizumab, for the first-line treatment of patients with advanced RCC
    - As a single agent, for the treatment of advanced renal cell carcinoma (RCC) after failure of one prior systemic therapy
  - Warnings and Precautions
    - Cardiac Failure: Monitor for signs or symptoms of cardiac failure throughout treatment with Inlyta
    - Hypertension and Hypertensive Crisis: Control blood pressure prior to initiating Inlyta. Monitor for hypertension and treat as needed. For persistent hypertension despite use of anti-hypertensive medications, reduce the Inlyta dose
    - Venous Thromboembolic Events: Closely monitor patients who are at increased risk for these events. Permanently discontinue Inlyta for severe venous thromboembolic events
    - Embryo-Fetal Toxicity: Can cause fetal harm. Advise patients of the potential risk to a fetus and use of effective contraception
  - Dosage
    - Dosage stratified by indication (can be found in TCR/PI)
  - Availability
    - 1 mg and 5 mg tablets

Oncology, Oral- Renal Cell Carcinoma

- **tivozanib (Fotivda)**
  - **March 2021: FDA approved Fotivda for the treatment of adults with relapsed or refractory advanced renal cell carcinoma (RCC) following ≥ 2 prior systemic therapies**
  - **Indications**
    - **Treatment of adult patients with relapsed or refractory advanced renal cell carcinoma (RCC) following two or more prior systemic therapies**
  - **Warnings and Precautions**
    - **Cardiac Failure: Monitor for signs or symptoms of cardiac failure throughout treatment with Fotivda**
    - **Hypertension and Hypertensive Crisis: Control blood pressure prior to initiating Fotivda. Monitor for hypertension and treat as needed. For persistent hypertension despite use of anti-hypertensive medications, reduce the Fotivda dose**
    - **Venous Thromboembolic Events: Closely monitor patients who are at increased risk for these events. Permanently discontinue Fotivda for severe venous thromboembolic events**
    - **Embryo-Fetal Toxicity: Can cause fetal harm. Advise patients of the potential risk to a fetus and use of effective contraception**
  - **Dosage**
    - **Recommended Dose: 1.34 mg once daily with or without food for 21 days on treatment followed by 7 days off treatment (28-day cycle) until disease progression or unacceptable toxicity**
  - **Availability**
    - **Capsules: 1.34 mg and 0.89 mg**

Oncology, Oral- Renal Cell Carcinoma

- **Generic**
  - **sorafenib – September 2020**
    - **FDA approved sorafenib by Mylan as the first AB-rated generic for Nexavar**

- **cabozantinib; nivolumab (Cabometyx; Opdivo)**
  - **January 2021: FDA approved expanded indication of cabozantinib (Cabometyx) and nivolumab (Opdivo) for use in combination for the first-line treatment of patients with advanced renal cell carcinoma.**

Magellan Rx MANAGEMENT℠

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Oncology, Oral – Skin

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

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Magellan Medicaid Administration

Oncology, Oral – Lung

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 2021, an estimated 235,760 new cases of lung cancer will be diagnosed, and 131,880 deaths are estimated to occur
  - Currently, 5-year survival is estimated to be 21.7%, an increase from 18.6% reported in 2019
  - Declines in lung cancer mortality in the US have been accelerating in recent years
  - From 2009 through 2013, lung cancer mortality declined 2.4%, but from 2014 through 2018, this decline more than doubled, resulting in a 5% 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
  - **Gavreto**
  - Gilotrif
  - Iressa
  - **Lorbrena**
  - Retevmo
  - Tabrecta
  - **Tagrisso**
  - Tarceva
  - Vizimpro
  - **Xalkori**
  - Zykadia

Oncology, Oral- Lung

- **pralsetinib (Gavreto)**
  - **September 2020: FDA approved pralsetinib (Gavreto), a kinase inhibitor, indicated for the treatment of adult patients with metastatic RET fusion-positive non-small cell lung cancer (NSCLC) as detected by an FDA approved test; continued approval may require demonstration of benefit in confirmatory clinical trials. Patients should be selected for treatment based on the presence of a RET gene fusion**
  - **December 2020: FDA granted Accelerated Approval for new indication for adult and peds ≥ 12 years old with advanced or metastatic RET-mutant medullary thyroid cancer (MTC) who require systemic therapy; and adult and ped patients ≥ 12 years old with advanced or metastatic RET fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate)**
  - **Warnings and Precautions**
    - **Interstitial Lung Disease (ILD)/Pneumonitis: Withhold Gavreto for Grade 1 or 2 reactions until resolution and then resume at a reduced dose. Permanently discontinue for recurrent ILD/pneumonitis. Permanently discontinue for Grade 3 or 4 reactions**
    - **Hepatotoxicity: Monitor ALT and AST prior to initiating Gavreto, every 2 weeks during the first 3 months, then monthly thereafter and as clinically indicated. Withhold, reduce dose, or permanently discontinue Gavreto based on severity**
    - **Embryo-Fetal Toxicity: Can cause fetal harm. Advise patients of the potential risk to a fetus and use of effective contraception**
    - **Pediatric Use: Monitor open growth plates in adolescent patients. Consider interrupting or discontinuing Gavreto if abnormalities occur**
  - **Dosage**
    - **The recommended dosage in adults and pediatric patients 12 years and older is 400 mg orally once daily on an empty stomach**
  - **Availability**
    - **Capsules: 100 mg**

Oncology, Oral- Lung

- **osimertinib (Tagrisso)**
  - **December 2020: New indication for use as adjuvant therapy after tumor resection in adult patients with non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test**
  - **Indications**
    - **Adjuvant therapy after tumor resection in adult patients with non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test**
    - The first-line treatment of adult patients with metastatic NSCLC whose tumors have EGFR exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test
    - The treatment of adult patients with metastatic EGFR T790M mutationpositive NSCLC, as detected by an FDA-approved test, whose disease has progressed on or after EGFR TKI therapy
  - **Warnings and Precautions**
    - Interstitial Lung Disease (ILD)/Pneumonitis: Occurred in 3.7% of patients. Permanently discontinue treatment in patients diagnosed 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 Tagrisso
    - Embryo-Fetal Toxicity: Can cause fetal harm. Advise patients of the potential risk to a fetus and use of effective contraception
  - **Dosage**
    - 80 mg orally once daily
  - **Availability**
    - **Tablets: 80 mg and 40 mg**

Oncology, Oral- Lung

- **crizotinib (Xalkori)**
  - **January 2021: FDA approved new indication in pediatrics ≥ 1 year of age and young adults with relapsed or refractory, systemic anaplastic large cell lymphoma (ALCL) that is anaplastic lymphoma kinase (ALK)-positive; its safety and efficacy have not been established in older adults with relapsed or refractory systemic ALK-positive ALCL. It was already approved for metastatic NSCLC whose tumors are ALK- or ROS1-positive as detected by an FDA-approved test**
  - **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**
    - Limitations of Use: The safety and efficacy of XALKORI have not been established in older adults with relapsed or refractory, systemic ALK-positive ALCL
  - **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**
    - Metastatic NSCLC: The recommended dosage is 250 mg orally twice appetite, pyrexia, abdominal pain, cough, and pruritus
    - **Systemic ALCL: The recommended dosage is 280 mg/m^2 orally twice**
  - **Availability**
    - Capsules: 250 mg, 200 mg

Oncology, Oral- Lung

- **tepotinib (Tepmetko)**
  - February 2021: FDA granted Accelerated Approval for tepotinib (Tepmetko), a kinase inhibitor, indicated for the treatment of adults with metastatic non-small cell lung cancer (NSCLC) harboring mesenchymal epithelial transition (MET) exon 14 skipping alterations
  - Indications
    - Treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) harboring mesenchymalepithelial transition (MET) exon 14 skipping alterations
    - 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 confirmatory trials
  - Warnings and Precautions
    - Interstitial Lung Disease (ILD)/Pneumonitis: Permanently discontinue in patients with ILD/pneumonitis
    - Hepatotoxicity: Monitor liver function tests. Withhold, dose reduce, or permanently discontinue Tepmetko based on severity
    - Embryo-Fetal Toxicity: Can cause fetal harm. Advise patients of the potential risk to a fetus and use of effective contraception
  - Dosage
    - Recommended dosage: 450 mg orally once daily with food until disease progression or unacceptable toxicity
  - Availability
    - Tablets: 225 mg

Oncology, Oral- Lung

- **lorlatinib (Lorbrena)**
  - **March 2021: The FDA approved indication was expanded from the initial Accelerated Approval for use in the 2nd or 3rd line setting to the following full approval: the treatment of adults with metastatic non-small cell lung cancer (NSCLC) whose tumors are anaplastic lymphoma kinase (ALK)-positive as detected by an FDA-approved test. Patients should be selected for treatment of metastatic NSCLC based on ALK positivity in tumor specimens**
  - **Indications**
    - **Treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are anaplastic lymphoma kinase (ALK)-positive as detected by an FDA-approved test**
  - **Warnings and Precautions**
    - **Risk of Serious Hepatotoxicity with Concomitant Use of Strong CYP3A Inducers: Discontinue strong CYP3A inducers for 3 plasma half-lives of the strong CYP3A inducer prior to initiating Lorbrena**
    - **Interstitial Lung Disease/Pneumonitis: Immediately withhold Lorbrena in patients with suspected ILD/pneumonitis. Permanently discontinue for treatment-related ILD/pneumonitis of any severity**
    - **Embryo-Fetal Toxicity: Can cause fetal harm. Advise patients of the potential risk to a fetus and use of effective contraception**
  - **Dosage**
    - **Recommended dosage: 100 mg orally once daily**
    - **Severe Renal Impairment: 75 mg orally once daily**
  - **Availability**
    - **Tablets: 25 mg or 100 mg**

Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Oncology, Oral – Other

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

- **tazemetostat (Tazverik)**
  - **June 2020: FDA approved Tazverik for the treatment of adults with relapsed or refractory (R/R) follicular lymphoma (FL) whose tumors are positive for an EZH2 mutation, as detected by an FDA-approved test, and who have received ≥ 2 prior systemic therapies, as well as for the treatment of adults with R/R FL who have no satisfactory alternative treatment options. Both indications for follicular lymphoma are approved based on Accelerated Approval; continued approval may be contingent on results of additional clinical trial data**
  - **Indications**
    - **The treatment of:**
      - Adults and pediatric patients aged 16 years and older with metastatic or locally advanced epithelioid sarcoma not eligible for complete resection
      - **Adult patients with relapsed or refractory follicular lymphoma whose tumors are positive for an EZH2 mutation as detected by an FDA-approved test and who have received at least 2 prior systemic therapies**
      - Adult patients with relapsed or refractory follicular lymphoma who have no satisfactory alternative treatment options
  - **Warnings and Precautions**
    - Secondary Malignancies: Increases the risk of developing secondary malignancies, including T-cell lymphoblastic lymphoma, myelodysplastic syndrome, and acute myeloid leukemia. Monitor patients long-term for the development of secondary malignancies
    - Embryo-Fetal Toxicity: Can cause fetal harm. Advise patients of the potential risk to a fetus and use of effective contraception
  - **Dosage**
    - **Recommended dosage is 800 mg taken orally twice daily with or without food**
  - **Availability**
    - **Tablets: 200 mg**

Oncology, Oral- Other

- **ripretinib (Qinlock)**
  - **July 2020: FDA approved ripretinib (Qinlock) a tyrosine kinase inhibitor indicated for the treatment of adults with advanced gastrointestinal stromal tumor (GIST) who have received prior treatment with ≥ 3 kinase inhibitors, including imatinib**
  - **Indications**
    - **Treatment of adult patients with advanced gastrointestinal stromal tumor (GIST) who have received prior treatment with 3 or more kinase inhibitors, including imatinib**
  - **Warnings and Precautions**
    - **Palmar-Plantar Erythrodysesthesia Syndrome: Based on severity, withhold Qinlock and resume at same or reduced dose**
    - **New Primary Cutaneous Malignancies: Perform dermatologic evaluations when initiating Qinlock and routinely during treatment**
    - **Hypertension: Do not initiate Qinlock in patients with uncontrolled hypertension and monitor blood pressure during treatment. Based on severity, withhold Qinlock and then resume at same or reduced dose or permanently discontinue**
    - **Embryo-Fetal Toxicity: Can cause fetal harm. Advise patients of the potential risk to a fetus and use of effective contraception**
  - **Dosage**
    - **Recommended Dosage: 150 mg orally once daily with or without food**
  - **Availability**
    - **Tablets: 50 mg**

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. The presence of an FGFR2 fusion or rearrangement should be confirmed before starting therapy**
  - **Indications**
    - **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**
    - **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 confirmatory trial(s)**
  - **Warnings and Precautions**
    - Hyperphosphatemia and Soft Tissue Mineralization: Increases in phosphate levels can cause hyperphosphatemia leading to soft tissue mineralization, cutaneous calcinosis, non-uremic calciphylaxis, vascular calcification, and myocardial calcification. Withhold, dose reduce, or permanently discontinue as recommended
    - Embryo-Fetal Toxicity: Can cause fetal harm. Advise patients of the potential risk to a fetus and use of effective contraception
  - **Dosage**
    - **Confirm the presence of an FGFR2 fusion or rearrangement prior to initiation of treatment**
    - **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- Other

- **avapritinib (Ayvakit)**
  - **June 2021: FDA approved expanded indication for the treatment of adults with aggressive systemic mastocytosis (ASM), systemic mastocytosis with an associated hematological neoplasm (SMAHN), and mast cell leukemia (MCL)**
  - **Indications**
    - Gastrointestinal Stromal Tumor (GIST)
      - The treatment of adults with unresectable or metastatic GIST harboring a platelet-derived growth factor receptor alpha (PDGFRA) exon 18 mutation, including PDGFRA D842V mutations
    - **Advanced Systemic Mastocytosis (AdvSM)**
      - **The treatment of adult patients with AdvSM. AdvSM includes patients with aggressive systemic mastocytosis (ASM), systemic mastocytosis with an associated hematological neoplasm (SMAHN), and mast cell leukemia (MCL)**
      - **Limitations of Use: Not recommended for the treatment of patients with AdvSM with platelet counts of less than 50 X 109 /L**
  - **Warnings and Precautions**
    - Intracranial Hemorrhage: Permanently discontinue for any occurrence of any grade
    - Embryo-Fetal Toxicity: Can cause fetal harm. Advise patients of the potential risk to a fetus and use of effective contraception
  - **Dosage**
    - GIST: Select patients for treatment based on the presence of a PDGFRA exon 18 mutation
    - GIST: The recommended dosage is 300 mg orally once daily
    - **AdvSM: The recommended dosage is 200 mg orally once daily**
  - **Availability**
    - Tablets: 25 mg, 50 mg, 100 mg, **200 mg** and 300 mg

Oncology, Oral- Other

- **New Diagnostic**
  - **larotrectinib (Vitrakvi)– October 2020**
    - **The FDA has approved a companion diagnostic for larotrectinib (Vitrakvi)**
    - **The companion diagnostics, a next-generation sequencing (NGS)-based FoundationOne CDx test can be used to identify fusions in neurotrophic receptor tyrosine kinase (NTRK) genes, NTRK1, NTRK2, and NTRK3, in DNA isolated from tumor tissue specimens from patients with solid tumors eligible for treatment with Larotrectinib**
  - **rucaparib (Rubraca)– October 2020**
    - **PI updated to instruct to select patient for metastatic castration-resistant prostate cancer (mCRPC) therapy based on FDA-approved companion diagnostic**
    - **If result is negative for BRCA mutations, considerer further genomic testing using tumor specimens.**

- **REMS Update**
  - **pexidartinib HCl (Turalio)- February 2021**
    - **REMS documents updated to list gamma-glutamyl transferase (GGT), alkaline phosphatase (ALP) elevations and direct bilirubin (DBIL) elevations as a trigger for liver adverse event reporting suggestive of serious and potentially fatal liver injury, and to align with the product label**

Appendices

Treatment Guidelines

The 2019 American College of Gastroenterology (ACG)

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

Treatment Guidelines

American Gastroenterology Association (AGA), 2019

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

Treatment Guidelines

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

Smoking Cessation Agents - Guidelines

- Clinical Practice Guidelines for Treating Tobacco Use and Dependence, 2008
  - All smokers who are trying to quit should be offered medication, except when contraindicated or for specific populations for which there is insufficient evidence of effectiveness (e.g., pregnant women, smokeless tobacco users, light smokers, and adolescents)
  - All 7 of the Food and Drug Administration (FDA)-approved medications for treating tobacco use are recommended as first-line therapies in these guidelines: bupropion sustained-release (SR) (Zyban), nicotine gum (Nicorette), nicotine inhaler (Nicotrol), nicotine lozenge (Nicorette), nicotine nasal spray (Nicotrol NS), nicotine patch (Nicoderm CQ), and varenicline (Chantix).
  - Shorter term use of the nicotine patch (12 weeks) with the nicotine inhaler, or bupropion sustained-release, also increases long-term abstinence rates relative to placebo treatments.
  - The higher-dose preparations of nicotine gum, patch, and lozenge have been shown to be effective in highly-dependent smokers
  - Unfortunately, there are no well-accepted algorithms to guide optimal selection among the first-line medications
  - Other pragmatic factors that may influence therapy selection include the likelihood of adherence, presence of dentures when considering use of the gum, and dermatitis when considering use of the patch
- U.S. Preventative Services Task Force, 2020
  - In April 2020, the USPSTF issued a recommendation for school-aged children and adolescents who have not started to use tobacco stating that primary care clinicians are recommended to provide interventions (e.g., education or brief counseling), in order to prevent tobacco use initiation in these individuals (Level B recommendation)
  - However, for school-aged children and adolescents who use tobacco, it was concluded the current evidence is inadequate to determine the benefits versus risks of primary care-feasible interventions regarding tobacco cessation (Level I [insufficient] recommendation)