Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Washington Pharmacy Advisory Committee Meeting

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Agenda Topics

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

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Multiple Sclerosis Agents

Multiple Sclerosis Agents – Disease State Description

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

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

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

National Medical Society, 2017

Multiple Sclerosis Agents – Disease State Description

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

National Medical Society, 2017

Multiple Sclerosis Agents

- ofatumumab (Kesimpta)
  - **September 2020: The FDA has approved a new indication for ofatumumab and a new brand name to correspond with the new use, Kesimpta. Kesimpta is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults**
  - **Indication**
    - **A CD20-directed cytolytic antibody indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults**
  - **Limitation**
    - **Infections: Delay KESIMPTA administration in patients with an active infection until the infection is resolved. Vaccination with live-attenuated or live vaccines is not recommended during treatment with KESIMPTA and after discontinuation, until B-cell repletion**
    - **Fetal Risk: May cause fetal harm based on animal data. Advise females of reproductive potential of the potential risk to a fetus and to use an effective method of contraception during treatment and for 6 months after stopping Kesimpta**
  - **Dosage**
    - **Initial Dosing: 20 mg administered at Week 0, 1, and 2**
    - **Subsequent Dosing: 20 mg administered monthly starting at Week 4**
  - **Availability**
    - **Injection: 20 mg/0.4 mL solution in a single-dose prefilled Sensoready pen**
    - **Injection: 20 mg/0.4 mL solution in a single-dose prefilled syringe**

Multiple Sclerosis Agents

- pegylated interferon beta-1a (Plegridy)
  - **February 2021: FDA approved an intramuscular route of administration and a corresponding prefilled syringe; dosage is the same as the SC formulation (125 mcg/0.5 mL every 14 days)**
  - **Indication**
    - An interferon beta indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults
  - **Limitation**
    - Hepatic injury: monitor liver function tests; monitor patients for signs and symptoms of hepatic injury; consider discontinuation of Plegridy if hepatic injury occurs
    - Depression and suicide: advise patients to report immediately any symptom of depression or suicidal ideation to their healthcare provider; consider discontinuation of Plegridy if depression occurs
  - **Dosage**
    - Recommended dose: 125 micrograms every 14 days
    - A healthcare professional should train patients in the proper technique for self-administering subcutaneous injections using the prefilled pen or syringe or intramuscular injections using the prefilled syringe
  - **Availability**
    - Subcutaneous Administration: Injection: 125 mcg/0.5 mL in a single-dose prefilled pen or single-dose prefilled syringe; Injection: 63 mcg/0.5 mL in a single-dose prefilled pen or single-dose prefilled syringe; Injection: 94 mcg/0.5 mL in a single-dose prefilled pen or single-dose prefilled syringe
    - **Intramuscular Administration: Injection: 125 mcg/0.5 mL solution in a single-dose prefilled syringe**

Multiple Sclerosis Agents

- ponesimod (Ponvory)
  - **March 2021: FDA approved Ponvory, a sphingosine 1-phosphate receptor modulator indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults**
  - **Indication**
    - **Treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults**
  - **Limitation**
    - **Infections: May increase the risk of infections. Obtain a complete blood count (CBC) before initiating treatment. Monitor for infection during treatment and for 1-2 weeks after discontinuation. Do not start Ponvory in patients with active infection**
    - **Liver Injury: Discontinue if significant liver injury is confirmed. Obtain liver function tests before initiating treatment**
  - **Dosage**
    - **Titration is required for treatment initiation**
    - **The recommended maintenance dosage is 20 mg taken orally once daily**
    - **First-dose monitoring is recommended for patients with sinus bradycardia, first- or second-degree [Mobitz type I] atrioventricular (AV) block, or a history of myocardial infarction or heart failure**
  - **Availability**
    - **Tablets: 2 mg, 3 mg, 4 mg, 5 mg, 6 mg, 7 mg, 8 mg, 9 mg, 10 mg, and 20 mg**

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Lipotropics, Other:

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

Lipotropics, Other - Disease State Description

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

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

National Center for Health Statistics Data Brief, 2018

Lipotropics, Other - Guidelines

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

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

Lipotropics, Other

- **evinacumab-dgnb (Evkeeza)**
  - **February 2021: The FDA has approved evinacumab-dgnb, angiopoietin-like 3 (ANGPTL3) inhibitor indicated as an adjunct to other low-density lipoprotein-cholesterol (LDL-C) lowering treatments for adults and pediatric patients ≥ 12 years with homozygous familial hypercholesterolemia (HoFH)**
  - **Indications:**
    - **As an adjunct to other low-density lipoprotein-cholesterol (LDL-C) lowering therapies for the treatment of adult and pediatric patients, aged 12 years and older, with homozygous familial hypercholesterolemia (HoFH)**
    - **Limitations of Use:**
      - **The safety and effectiveness have not been established in patients with other causes of hypercholesterolemia, including those with heterozygous familial hypercholesterolemia (HeFH)**
      - **The effects on cardiovascular morbidity and mortality have not been determined**
  - **Warning & Precautions**
    - **Embryo-Fetal Toxicity: May cause fetal harm based on animal studies. Advise patients who may become pregnant of the risk to a fetus. Consider obtaining a pregnancy test prior to initiating treatment. Advise patients who may become pregnant to use contraception during treatment and for at least 5 months following the last dose**
  - **Dosage:**
    - **The recommended dose is 15 mg/kg administered by intravenous (IV) infusion once monthly (every 4 weeks)**
  - **Formulations:**
    - **Injection: 345 mg/2.3 mL (150 mg/mL) and 1,200 mg/8 mL (150 mg/mL) solution in single-dose vials**

Lipotropics, Other

- **alirocumab (Praluent)**
  - **April 2021: FDA Approved a new indication as an adjunct to other LDL-C-lowering therapies in adult patients with homozygous familial hypercholesterolemia (HoFH) to reduce LDL-C**
  - **Indications:**
    - To reduce the risk of myocardial infarction, stroke, and unstable angina requiring hospitalization in adults with established cardiovascular disease
    - As adjunct to diet, alone or in combination with other low-density lipoprotein cholesterol (LDL-C)-lowering therapies, in adults with primary hyperlipidemia, including heterozygous familial hypercholesterolemia (HeFH), to reduce LDL-C
    - **As an adjunct to other LDL-C-lowering therapies in adult patients with homozygous familial hypercholesterolemia (HoFH) to reduce LDL-C**
  - **Dosage:**
    - **In adults with HeFH undergoing LDL apheresis or in adults with HoFH: The recommended dose is 150 mg once every 2 weeks administered subcutaneously**
    - **Can be administered without regard to the timing of LDL apheresis**
  - **Formulations:**
    - Injection: 75 mg/mL or 150 mg/mL in a single-dose pre-filled pen

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Antivirals, Oral:

ANTIVIRALS : INFLUENZA AGENTS

Antivirals, Oral- Disease State Description

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

- Influenza vaccination is the primary method for preventing influenza
  - Inactivated influenza vaccines are available in quadrivalent and trivalent formulations, while recombinant influenza vaccine and LAIV4 are available in quadrivalent formulations
  - There is also a high-dose inactivated influenza vaccine and adjuvanted inactivated influenza vaccine available in trivalent formulations
  - For the 2020-2021 season, inactivated influenza vaccines, recombinant influenza vaccine, and live attenuated influenza vaccine (LAIV) are available
  - Virus strains included in the 2020-2021 US egg-based trivalent influenza vaccines contain hemagglutinin (HA) derived from an influenza A/Guangdong-Maonan/SWL1536/2019 (H1N1)pdm09-like virus, an A/Hong Kong/2671/2019 (H3N2)-like virus, and a B/Washington/02/2019 (Victoria lineage)-like virus Quadrivalent influenza vaccines contain HA derived from the 3 viruses contained in the trivalent vaccine plus a B/Phuket/3073/2013–like virus (Yamagata lineage)
  - Cell culture–based inactivated (ccIIV4) and recombinant (RIV4) influenza vaccines contain HA derived from an A/Hawaii/70/2019 (H1N1)pdm09-like virus, an A/Hong Kong/45/2019 (H3N2)-like virus, a B/Washington/02/2019 (Victoria lineage)-like virus, and a B/Phuket/3073/2013 (Yamagata lineage)-like virus

Centers for Disease Control and Prevention, 2020

Antivirals, Oral- Treatment Guidelines

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

Antivirals, Oral- Treatment Guidelines

- baloxavir marboxil (Xofluza)
  - **December 2020: FDA approved expanded indication for baloxavir marboxil tablets to include post-exposure prophylaxis of influenza in adults and pediatric patients ≥ 12 years old**
  - **December 2020: FDA approved a 40 mg/20 mL oral suspension for constitution to a final concentration of 2 mg/mL**
  - **Indications**
    - **Treatment of acute uncomplicated influenza in patients 12 years of age and older who have been symptomatic for no more than 48 hours and who are: otherwise, healthy, or at high risk of developing influenza-related complications**
    - **Post-exposure prophylaxis of influenza in patients 12 years of age and older following contact with an individual who has influenza**
  - **Warnings and Precautions**
    - Co-administration of baloxavir marboxil (Xofluza) with polyvalent cation-containing laxatives, antacids, or oral supplements (e.g., calcium, iron, magnesium, selenium, or zinc) should be avoided
  - **Dosage**
    - Adults:
      - In patients weighing 40 kg to < 80 kg, a single dose of 40 mg is recommended
      - In patients weighing ≥ 80 kg, 80 mg is recommended
  - **Availability**
    - Tablets: 20 and 40 mg
    - **For oral suspension: 40 mg/20 mL when constituted for final concentration of 2 mg/mL**

Antivirals, Oral- Treatment Guidelines

- peramivir (Rapivab)
  - **February 2021: FDA approved expanded indication for the treatment of acute uncomplicated influenza to patients ≥ 6 months of age (previously ≥ 2 years old) who have been symptomatic for ≤ 2 days**
  - **Indications**
    - Treatment of acute uncomplicated influenza in patients **6 months and older** who have been symptomatic for no more than two days
  - **Warnings and Precautions**
    - No recommendation for dosage adjustment can be made for pediatric patients 6 months to less than 2 years of age with creatinine clearance less than 50 mL/min
    - Hemodialysis: Administer after dialysis
    - Live attenuated influenza vaccine (LAIV), intranasal: Avoid use of LAIV within 2 weeks before or 48 hours after administration of Rapivab, unless medically indicated
  - **Dosage**
    - Adults Patients (≥ 13 years old): 600 mg
    - Pediatric Patients: 12 mg/kg (up to 600 mg)
  - **Availability**
    - Injection: 200 mg in 20 mL (10 mg/mL) in a single-use vial

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Sinus Node Inhibitors:

CARDIOVASCULAR AGENTS : SINUS NODE INHIBITORS

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Pituitary Suppressive Agents, LHRH:

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

Pituitary Suppressants - Disease State Description

- Prostate Cancer
  - From 2013 to 2017, the median age at diagnosis of prostate cancer in the US was 66 years
  - The estimated number of new cases of prostate cancer in the US in 2020 is 191,930 with estimated deaths at 33,330

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

Pituitary Suppressants

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

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Ulcerative Colitis Agents:

GASTROINTESTINAL AGENTS : INFLAMMATORY BOWEL AGENTS

Ulcerative Colitis - Disease State Description

- **Ulcerative Colitis (UC)**
  - A chronic inflammatory disease primarily affecting the colon and rectum
  - 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
  - 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

Ulcerative Colitis – Treatment Guidelines

American Gastroenterology Association (AGA), 2020

- Moderate to severe UC
  - Consider 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

Ulcerative Colitis Agents

- ozanimod hydrochloride (Zeposia)
  - **May 2021: FDA has approved Zeposia for the treatment of moderately to severely active ulcerative colitis (UC) in adults. Zeposia was already indicated for adults with relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease**
  - **Indication**
    - Relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults
    - **Moderately to severely active ulcerative colitis (UC) in adults**
  - **Limitation**
    - Infections: May increase the risk of infections. Obtain a complete blood count (CBC) before initiating treatment. Monitor for infection during treatment and for 1-2 weeks after discontinuation. Do not start Zeposia in patients with active infection
    - Liver Injury: Discontinue if significant liver injury is confirmed. Obtain liver function tests before initiating treatment
    - Vaccination: Avoid use of live attenuated vaccines during and for up to 3 months after treatment with Zeposia
    - Fetal Risk: Women of childbearing potential should use effective contraception during treatment and for 3 months after stopping Zeposia
  - **Dosage**
    - The recommended maintenance dosage is 0.92 mg orally once daily
    - If a dose is missed within the first 2 weeks of treatment, reinitiate with the titration regimen. If a dose is missed after the first 2 weeks of treatment, continue treatment as planned
  - **Availability**
    - Capsules: 0.23 mg, 0.46 mg, 0.92 mg ozanimod

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GI Motility, Chronic:

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

GI Motility, Chronic- Disease State Description

- Constipation
  - A syndrome that is defined by bowel symptoms specific to the difficult passage of stool, infrequent passage of stool, abnormal hardness of stool, or a feeling of incomplete evacuation after a bowel movement
  - Though constipation can occur secondary to another disease (e.g., Parkinson's disease, spinal cord injury), idiopathic constipation occurs independent of any other underlying disorder
  - Chronic idiopathic constipation (CIC) is diagnosed if there are < 3 spontaneous bowel movements (SBMs) per week with symptoms occurring for ≥ 6 months and at least 2 of the previously mentioned bowel symptoms

American Gastroenterological Association, 2013

GI Motility, Chronic- Disease State Description

- Irritable bowel syndrome (IBS)
  - A functional bowel disorder which can be chronic, relapsing, and often life-long
  - Occurs in up to 15% of the population and is up to 2.5 times more common in women than men
  - Characterized by symptoms of abdominal pain or discomfort associated with abnormal stool frequency, abnormal stool consistency, abnormal stool passage, and/or bloating or abdominal distension, which may or may not be relieved by defecation, at least 3 days per month in the past 3 months
    - Can also present with non-colonic features (e.g., functional urinary and gynecologic problems, gallbladder and stomach symptoms, back pain, migraine, and depression) which can lead to inappropriate patient referrals
  - Patients present with a combination of symptoms that are typically constipation predominant (IBS-C), diarrhea predominant (IBS-D), and/or alternating between both, or mixed (IBS-M)
  - Causes have not been fully identified, but could potentially include gut hypersensitivity, disturbed colonic motility, post-infective bowel dysfunction, or a defective anti-nociceptive system
  - There may also be contributing factors (e.g., stress, food intolerance, abnormal intestinal flora) which can hinder the effectiveness of treatment if left unresolved

American Gastroenterological Association, 2013

GI Motility, Chronic

- lubiprostone
  - **January 2021: First authorized generic for Mallinckrodt's Amitiza from Par**
  - Indications:
    - Chronic idiopathic constipation (CIC) in adults
    - Opioid-induced constipation (OIC) in adult patients with chronic, non-cancer pain, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g., weekly) opioid dosage escalation
    - Irritable bowel syndrome with constipation (IBS-C) in women ≥18 years old
  - Limitations:
    - Nausea: Patients may experience nausea; concomitant administration of food may reduce this symptom
    - Diarrhea: Avoid use in patients with severe diarrhea. Instruct patients to discontinue Amitiza and contact their healthcare provider if severe diarrhea occurs during treatment
  - Dosing:
    - CIC and OIC: 24 mcg twice daily
    - IBS-C: 8 mcg twice daily
  - Formulations:
    - Capsules: 8 mcg and 24 mcg

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Phosphate Binders:

GASTROINTESTINAL AGENTS : PHOSPHATE BINDER AGENTS

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Bladder Relaxant Preparations:

GENITOURINARY AGENTS : OVERACTIVE BLADDER AGENTS

Bladder Relaxant Preparations - Disease State Description/Treatment

- **Overactive bladder (OAB)**
  - A chronic and debilitating syndrome that is characterized by urinary urgency with or without urge incontinence, usually in combination with urinary frequency (8 or more voiding episodes per 24 hours) and nocturia (awakening 1 or more times per night to void)
  - Prevalent in ~16% of men and 17% of women
  - ~20% in those older than 60 years of age

- Treatment
  - 1st line therapy: Behavioral therapy
  - 2nd line therapy: Oral antimuscarinics including darifenacin, fesoterodine, oxybutynin, solifenacin, tolterodine, or trospium
  - Surgery is reserved for patients with severe refractory OAB symptoms or who are not candidates for oral therapy

The American Urological Association (AUA), 2014

Bladder Relaxant Preparations

- **vibegron (Gemtesa)**
  - **December 2020: FDA approved vibegron (Gemtesa), a beta-3 adrenergic agonist indicated for the treatment of overactive bladder (OAB) with symptoms of urge urinary incontinence, urgency, and urinary frequency in adults**
  - **Indications:**
    - **The treatment of overactive bladder (OAB) with symptoms of urge urinary incontinence, urgency, and urinary frequency in adults**
  - **Precautions/Contraindications:**
    - **Urinary Retention: Monitor for urinary retention, especially in patients with bladder outlet obstruction and in patients taking muscarinic antagonist medications for OAB, in whom the risk of urinary retention may be greater. If urinary retention develops, discontinue treatment**
    - **Pediatric use: Safety and effectiveness in pediatric patients have not been established**
    - **End-stage Renal Disease with or without Hemodialysis: Not recommended**
    - **Severe Hepatic Impairment: Not recommended**
  - **Dosage:**
    - **The recommended dose is one 75 mg tablet once daily**
  - **Formulations:**
    - **Tablets: 75 mg**

Bladder Relaxant Preparations

- **mirabegron (Myrbetriq)**
  - **April 2021: FDA approved Myrbetriq for the treatment of neurogenic detrusor overactivity (NDO) in pediatric patients aged ≥ 3 years old. Previously, it was approved for use only in adults with overactive bladder**
  - **April 2021: FDA also approved a new dosage form for use in this younger population, Myrbetriq granules, an extended-release oral suspension with a strength of 8 mg/mL following reconstitution. Myrbetriq was already approved as an extended-release tablet (25 mg, 50 mg)**
  - **Indications:**
    - Overactive bladder (OAB) in adult patients with symptoms of urge urinary incontinence, urgency, and urinary frequency, either alone or in combination with the muscarinic antagonist solifenacin succinate
    - Neurogenic detrusor overactivity (NDO) in pediatric patients aged 3 years and older and weighing 35 kg or more
    - **Myrbetriq Granules is a beta-3 adrenergic agonist indicated for the treatment of NDO in pediatric patients aged 3 years and older**
  - **Precautions/Contraindications:**
    - Urinary Retention in Patients With Bladder Outlet Obstruction and in Patients Taking Muscarinic Antagonist Drugs for Overactive Bladder: Administer with caution in these patients because of risk of urinary retention
    - Angioedema: Angioedema of the face, lips, tongue, and/or larynx has been reported with mirabegron
  - **Dosage:**
    - Stratified by indication and age (found in TCR and/or PI)
  - **Formulations:**
    - Extended-release tablets: 25 mg and 50 mg
    - **For extended-release oral suspension: 8 mg/mL of mirabegron after reconstitution**

Bladder Relaxant Preparations

- **fesoterodine fumarate (Toviaz)**
  - **June 2021: FDA approved Toviaz for the treatment of neurogenic detrusor overactivity (NDO) in pediatric patients ≥ 6 years old and ≥ 25 kg. Previously, it was only approved for the treatment of overactive bladder in adults**
  - **Indications:**
    - Overactive bladder (OAB) in adults with symptoms of urge urinary incontinence, urgency, and frequency
    - **Neurogenic detrusor overactivity (NDO) in pediatric patients 6 years of age and older and weighing greater than 25 kg**
  - **Precautions/Contraindications:**
    - Angioedema: Promptly discontinue Toviaz and provide appropriate therapy
    - Urinary Retention: Toviaz is not recommended in patients with clinically significant bladder outlet obstruction because of the risk of urinary retention
    - Decreased Gastrointestinal Motility: Toviaz is not recommended for use in patients with decreased gastrointestinal motility, such as those with severe constipation
  - **Dosage:**
    - OAB in Adults: The recommended starting dosage is 4 mg orally once daily. Based upon individual response and tolerability, increase to the maximum dosage of 8 mg once daily
    - **NDO in Pediatric Patients 6 Years and Older:**
      - **Pediatric Patients Weighing Greater than 25 kg and up to 35 kg: The recommended dosage is 4 mg orally once daily. If needed, dosage may be increased to 8 mg orally once daily**
      - **Pediatric Patients Weighing Greater than 35 kg: The recommended starting dosage is 4 mg orally**
  - **Formulations:**
    - Extended-release tablets: 4 mg and 8 mg

Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

HAE Treatments:

HEMATOLOGICAL AGENTS : HEREDITARY ANGIOEDEMA AGENTS

Hereditary Angioedema – Disease State Description

- **Hereditary angioedema (HAE)**
  - A rare dominant, autosomal genetic disorder that affects ~ 6,000 individuals in the United States
  - Characterized by recurrent episodes of nonpruritic, nonpitting, subcutaneous or submucosal edema involving the skin or mucosal tissues of the upper respiratory and gastrointestinal (GI) tracts
  - Although swelling can resolve spontaneously in several days, without treatment, laryngeal edema may be fatal and the pain of GI attacks can be incapacitating
  - Symptoms can begin as early as 2 years of age and persist throughout life with unpredictable severity and frequency of attacks
    - It is thought that minor trauma and stress can lead to an attack; however, many attacks can occur without any apparent trigger
  - There are 2 types of C1-INH deficient HAE
    - Type I
      - The most common type
      - In which the body does not produce enough C1-INH, occurs in about 85% of patients with the condition
    - Type II
      - Characterized by the presence of normal or high levels of a dysfunctional C1-INH
  - HAE prophylaxis is needed to reduce potential edema caused by a stressor or procedure likely to precipitate an attack (short-term prophylaxis) or decrease the number of severity of angioedema attacks (long-term prophylaxis)

US Hereditary Angioedema Association, 2020

Hereditary Angioedema – Treatment Guidelines

- US Hereditary Angioedema Association (HAEA), 2020
  - Recommendations state than an accurate diagnosis of HAE must be established prior to discussing treatment options
    - An accurate diagnosis may be accomplished by measurement of serum C4 and assessment of C1-INH activity (functional and quantitative)
  - Additionally, treatment strategies should be individualized based primarily on patient specific factors such as age, comorbidities, and access to emergency medical facilities
  - Goal of treatment in children with HAE is to prevent mortality, minimize morbidity, and to allow for a normal childhood
  - Guidelines include four guiding principles: available on-demand acute therapy for all patients, early treatment to prevent attack progression, treatment of attack irrespective of the site of swelling, and individualized long-term prophylaxis
    - The guidelines recommend a single dose of pdC1-INH (Cinryze or Haegarda) or a course of anabolic androgen as the treatment of choice for children and adults for short-term prophylaxis prior to medical, surgical, or dental procedures
    - For long-term prophylaxis in children and adults, the guidelines recommend intravenous pdC1-INH (Cinryze), subcutaneous pdC1-INH (Haegarda), and monoclonal antibody lanadelumab-flyo (Takhyzro), a plasma kallikrein inhibitor, as first line therapy
  - If first line therapy is not available or the patient will only accept oral therapy, anabolic androgen and antifibrinolytics can be utilized as second line treatment options
  - For on-demand acute therapy in children and adults, the guidelines recommend one of the four medications FDA approved for use to treat HAE attacks: intravenous pdC1-INH (Berinert), intravenous rhC1-INH (Ruconest), subcutaneous plasma kallikrein inhibitor ecallantide (Kalbitor), and the subcutaneous bradykinin B2 receptor antagonist icatibant (Firazyr)

Hereditary Angioedema

- **C1 esterase inhibitor subcutaneous (human) (Haegarda)**
  - **In October 2020, the indication had been expanded to include peds patients ≥ 6 years of age for routine prophylaxis to prevent Hereditary Angioedema (HAE) attacks**
  - **Indication**
    - **Routine prophylaxis to prevent Hereditary Angioedema (HAE) attacks in patients 6 years of age and older**
  - **Warnings and Precautions**
    - Severe hypersensitivity reactions may occur
    - At the recommended subcutaneous (S.C.) dose, a causal relationship between thromboembolic events (TEEs) and the use of Haegarda has not been established. However, thrombosis has occurred in treatment attempts with high doses of C1-INH intravenous (I.V.) for prevention or therapy of capillary leak syndrome before, during or after cardiac surgery (unapproved indication and dose)
  - **Dosage**
    - Administer 60 International Units per kg body weight twice weekly (every 3 or 4 days)
  - **Availability**
    - White lyophilized powder supplied in single-dose vials containing 2000 or 3000 International Units (IU) of C1-INH

Hereditary Angioedema

- **berotralstat (Orladeyo)**
  - **In December 2020, FDA approved Orladeyo, a plasma kallikrein inhibitor indicated for prophylaxis to prevent attacks of hereditary angioedema (HAE) in adults and pediatric patients ≥ 12 years old**
  - **Indication**
    - **Prophylaxis to prevent attacks of hereditary angioedema (HAE) in adults and pediatric patients 12 years and older**
    - **Limitations of Use: Should not be used for treatment of acute HAE attacks**
  - **Warnings and Precautions**
    - **An increase in QT prolongation can occur at dosages higher than the recommended 150 mg once daily dosage. Additional doses or doses of ORLADEYO higher than 150 mg once daily are not recommended**
    - **Dosage adjustment in patients with moderate or severe hepatic impairment**
    - **Dosage adjustment in patients with chronic administration of P-gp or BCRP inhibitors**
    - **Dosage adjustment in patients with persistent gastrointestinal reactions**
  - **Dosage**
    - **Recommended Dosage: One capsule (150 mg) taken orally once daily with food**
  - **Availability**
    - **Capsules: 150 mg, 110 mg**

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Potassium Binders:

MISCELLANEOUS THERAPEUTIC CLASSES : POTASSIUM REMOVING AGENTS

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Opiate Dependence Treatments:

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

Opiate Dependence Treatment – Disease State Description

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

- The 2019 National Survey on Drug Use and Health (NSDUH) reported there was an estimated 35.8 million Americans aged 12 years and older who were current (past month) illicit drug users
  - There were approximately 1.6 million people aged 12 or older in the United States (US) who misused opioids in the past year
  - Approximately 20.4 million people aged 12 or older in 2019 were considered to have a substance use disorder (SUD) in the past year, including 14.5 million people with an alcohol use disorder, 8.3 million people with an illicit drug use disorder, and 1.6 million had an opioid use disorder

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

Opiate Dependence Treatment – Guidelines

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

Opiate Dependence Treatment – Guidelines

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

Opiate Dependence Treatment

- FDA, 2020
  - The FDA has released a drug safety communication and a MedWatch for opioid pain relievers and opioid use disorder (OUD) agents
    - Requiring manufacturers for all opioid pain relievers and OUD treatments (e.g., buprenorphine, methadone and naltrexone) add recommendations on naloxone to the product labeling for Healthcare Practitioners to consider and discuss prescribing naloxone
    - Recommending Healthcare Practitioners discuss and consider naloxone use with all patients at the time of prescribing
    - Recommends Healthcare Practitioners consider prescribing naloxone when a patient has household members (e.g., children, close contacts) who may be at risk for accidental ingestion or opioid overdose
      - In addition, for patients that are not receiving a prescription for an opioid analgesic or OUD treatment, consideration should be given to prescribing naloxone for them if they are at a higher risk of opioid overdose (e.g., current/prior diagnosis of OUD or prior opioid overdose)
  - When these meds are prescribed or renewed, the FDA is recommending the potential need for a naloxone prescription to be evaluated

Opiate Dependence Treatment

- naloxone nasal (Kloxxado)
  - **April 2021: FDA approved a new higher dose naloxone HCl nasal spray that delivers 8 mg naloxone to treat opioid overdose. Previously approved as 2 mg and 4 mg naloxone nasal spray products**
  - **Indication**
    - The emergency treatment of known or suspected opioid overdose, as manifested by respiratory and/or central nervous system depression, for adult and pediatric patients
    - Intended for immediate administration as emergency therapy in settings where opioids may be present
    - Not a substitute for emergency medical care
  - **Limitation**
    - Risk of Recurrent Respiratory and CNS Depression: Due to the duration of action of naloxone relative to the opioid, keep patient under continued surveillance and administer repeat doses of naloxone using a new nasal spray with each dose, as necessary, while awaiting emergency medical assistance
  - **Dosage**
    - Administer a single spray to adult or pediatric patients intranasally into one nostril
    - Administer additional doses, using a new nasal spray with each dose, if the patient does not respond or responds and then relapses into respiratory depression. Additional doses may be given every 2 to 3 minutes until emergency medical assistance arrives
  - **Availability**
    - **Nasal spray: naloxone hydrochloride 8 mg in 0.1 mL**

Appendices

Multiple Sclerosis Agents – Guidelines

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

GI Motility, Chronic - Treatment Guidelines

- Opioid-induced constipation (OIC) is a common adverse effect of opioid therapy
  - American Pain Society (APS) and American Academy of Pain Medicine (AAPM), 2009
    - Recommend that patients receiving chronic opioid therapy with non-cancer pain that have common adverse effects, including constipation, should be anticipated and addressed appropriately
  - American Society of Interventional Pain Physicians (ASIPP), 2012
    - Recommend for patients receiving chronic non-cancer pain medications to be initiated on a prophylactic bowel regimen (e.g., increased fluid and fiber intake, stool softeners, laxatives) before the development of constipation and definitely after its development
  - American Gastroenterological Association, 2019
    - Recommends use of traditional laxatives as first-line agents
    - However, in patients with laxative refractory OIC, it is recommended that peripherally acting mu-opioid receptor antagonists (PAMORAs), such as naldemedine and naloxegol, are utilized over no treatment
    - Methylnaltrexone (Relistor) is suggested over no treatment, but this was given a conditional recommendation due to low quality of evidence
    - Additionally, the guidelines makes no recommendations for intestinal secretagogues (e.g., lubiprostone [Amitiza]) or 5-HT agonists (e.g. prucalopride [Motegrity]) due to limited consistent evidence to support their use

Ulcerative Colitis – 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

Ulcerative Colitis – 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