Medical management of low-risk adult patients with mild to moderate ulcerative colitis

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INTRODUCTION

Ulcerative colitis (UC) is a chronic inflammatory condition characterized by relapsing episodes of inflammation limited to the mucosal layer of the colon. The rectum is usually affected, and inflammation may extend in a proximal and continuous fashion to involve other portions of the colon.

This topic will review the medical management of mild to moderate UC. Health maintenance for patients with inflammatory bowel disease (IBD) is also discussed. The management of high-risk patients with moderate to severe UC is discussed separately. (See "Management of moderate to severe ulcerative colitis in adults".)

The management of patients with acute, severe UC is discussed separately. (See "Management of the hospitalized adult patient with severe ulcerative colitis".)

The surgical management of UC is discussed separately. (See "Surgical management of ulcerative colitis".)

The clinical manifestation and diagnosis of UC are discussed separately. (See "Clinical manifestations, diagnosis, and prognosis of ulcerative colitis in adults".)

Adjustments to medication regimens for patients with IBD and suspected or known coronavirus disease 19 (COVID-19) are discussed separately. (See "COVID-19: Issues related to

gastrointestinal disease in adults".)

The American Gastroenterological Association and the American College of Gastroenterology have published guidelines on management of UC [1-3]. Our approach is generally consistent with society guidelines; however, if differences exist, they are noted.

DISEASE ACTIVITY, SEVERITY, AND RISK

Defining disease activity — Clinical trials of UC often use formal grading systems to describe disease activity. The severity of UC is generally classified as mild, moderate, or severe disease; however, the definition of mild to moderate disease activity may vary in the literature depending on the specific index or score being used (eg, Truelove and Witts severity index [4], Mayo Clinic score [5], Montreal classification [6]).

In clinical practice, the following definitions may be more useful:

- **Mild** – Patients with mild clinical disease have ≤4 stools per day with or without small amounts of blood, no signs of systemic toxicity (eg, no tachycardia), and a normal C-reactive protein (CRP) and/or erythrocyte sedimentation rate (ESR). Mild crampy abdominal pain, tenesmus, and periods of constipation are also common, but severe abdominal pain, profuse bleeding, fever, and weight loss are not part of the spectrum of mild disease.

- **Moderate** – Patients with moderate clinical disease may have frequent (four to six per day), loose, bloody stools, mild anemia not requiring blood transfusions (hemoglobin >10 g/dL), and abdominal pain that is not severe. Patients have no or minimal signs of systemic toxicity. Adequate nutrition is usually maintained and weight loss is not associated with moderate clinical disease.

- **Severe** – Patients with a severe clinical disease typically have frequent, loose bloody stools (≥6 per day) with severe cramps and evidence of systemic toxicity as demonstrated by a fever (temperature ≥37.8°C), tachycardia (heart rate ≥90 beats per minute), anemia (hemoglobin <10 g/dL), and/or an elevated CRP or ESR. Patients may have weight loss. The management of acute, severe UC is discussed separately. (See "Management of the hospitalized adult patient with severe ulcerative colitis".)

Defining disease extent — Terminology to describe the extent of involvement of UC includes [2]. (See "Endoscopic diagnosis of inflammatory bowel disease in adults", section on 'Differentiating ulcerative colitis from Crohn disease'.):

- **Ulcerative proctitis** – Ulcerative proctitis refers to disease within 18 cm of the anal verge, distal to the rectosigmoid junction
- **Ulcerative proctosigmoiditis** – Ulcerative proctosigmoiditis refers to disease limited to the rectum and sigmoid colon and not involving the descending colon
- **Left-sided colitis** – Left-sided colitis refers to disease that extends beyond the sigmoid colon and as far proximally as the splenic flexure
- **Extensive colitis** – Extensive colitis refers to disease extending proximal to the splenic flexure

Colonoscopy is required to determine the extent of involvement, and the distribution of mucosal inflammation may progress over time [7,8].

Low- versus high-risk patients — In addition to the clinical parameters, the American Gastroenterological Association stratifies patients into either a low or high risk category by assessing inflammatory status with the following tests [1]:

- Endoscopic evaluation for mucosal ulcerations and disease extent
- Laboratory studies (eg, fecal calprotectin)

For patients with mild to moderate UC, the following features may predict a lower risk for long-term sequelae (eg, colectomy) [1,9,10]. (See 'Defining disease extent' above.):

- Mild or moderate symptoms (≤6 stools daily with or without blood)
- No systemic symptoms (eg, fever, weight loss)
- Lack of severe endoscopic disease (eg, lack of deep ulcerations)
- Normal or mild elevation in CRP, ESR, and/or fecal calprotectin levels
- No extraintestinal manifestations
- Diagnosis at age >40 years
- Normal albumin

Patients initially identified as low risk may be subsequently reclassified as high risk if they develop complications or do not respond to initial treatment. Other prognostic factors associated with a more complicated disease course include number of flares, need for glucocorticoids, number of hospitalizations related to UC, and infection with *Clostridioides difficile* or cytomegalovirus [9,10].

Management of high-risk, ambulatory patients with moderate to severe UC or patients with acute severe UC is discussed separately. (See "Management of moderate to severe ulcerative colitis in adults" and "Management of the hospitalized adult patient with severe ulcerative colitis".)

PRETREATMENT EVALUATION

Therapy for UC is guided by pretreatment evaluation (laboratory studies and lower endoscopy), and the goals are to exclude alternative or coexisting conditions and determine the extent and severity of disease.

When a patient with UC presents with symptoms of a disease flare (eg, diarrhea, rectal bleeding), some aspects of the initial evaluation (eg, laboratory and stool studies, lower endoscopy) should be repeated to exclude other conditions as a cause for symptoms and to assess the extent and severity of disease. We begin by assessing the patient's risk factors for other etiologies of colitis, such as use of nonsteroidal anti-inflammatory drugs or antibiotics, recent travel to endemic areas, or ingestion of raw meat or fish.

Our approach to diagnostic testing includes the following:

- **Laboratory testing** – We typically obtain complete blood count, liver biochemical tests, albumin, and C-reactive protein (CRP). While CRP as a serologic marker of inflammation has largely replaced ESR, both may be sent in combination, and in rare circumstances, clinicians may only have access to ESR [11-13]. For example, a normal CRP in a patient with recurrent symptoms (who previously had elevated CRP in the setting of active mucosal inflammation) suggests a noninflammatory etiology (eg, functional symptoms) [13-15]. (See "Approach to functional gastrointestinal symptoms in adults with inflammatory bowel disease", section on 'Evaluation'.)

- **Stool studies** – We typically obtain stool testing for inflammation (ie, fecal calprotectin) and for infection (ie, *Clostridioides* [formerly *Clostridium*] *difficile*, routine stool cultures [*Salmonella*, *Shigella*, *Campylobacter*, *Yersinia*], and specific testing for *E. coli* O157:H7). For patients with risk factors for parasitic infection (eg, recent travel to a region where parasitic infections are endemic), stool microscopy for ova and parasites (three specimens) and a *Giardia* stool antigen test are also checked. Stool analysis for the detection of pathogens is discussed in more detail separately:

  - (See "*Clostridioides difficile* infection in adults: Clinical manifestations and diagnosis", section on 'Diagnosis'.)

- (See "Approach to the adult with acute diarrhea in resource-abundant settings".)
- (See "Giardiasis: Epidemiology, clinical manifestations, and diagnosis".)
- (See "Approach to stool microscopy".)

- **Approach to lower endoscopy** – Lower endoscopy may be needed, and the approach to repeating the endoscopic evaluation depends on the time interval between the patient's previous lower endoscopy and the onset of symptoms, the severity of the patient's symptoms, and duration of symptoms. (See 'Defining disease activity' above and "Management of moderate to severe ulcerative colitis in adults", section on 'Defining overall disease activity'.)

- **Patients without severe symptoms** – We typically perform colonoscopy for ambulatory patients without severe symptoms (eg, <6 stools daily with or without blood, no systemic symptoms) who have had their previous colonoscopy (or flexible sigmoidoscopy) >6 months prior to presentation. A flexible sigmoidoscopy is an acceptable alternative, particularly for patients who have a history of disease limited to distal colon.

  For patients without severe symptoms who have had a colonoscopy within the previous six months, we use inflammatory markers (CRP and fecal calprotectin) to reassess disease activity. Inflammatory markers with values within the reference range generally indicate that mucosal disease has remained in remission, and this usually obviates the need for repeating endoscopic evaluation. If an inflammatory marker is elevated, we generally initiate treatment for a flare of UC without repeating endoscopic evaluation.

- **Ambulatory patients with severe symptoms** – We typically perform lower endoscopy without bowel preparation for patients with severe gastrointestinal symptoms (eg, frequent loose bloody stools [≥6 per day]) because they may require escalation of therapy. Lower endoscopy with mucosal biopsies is typically performed to assess the severity and extent of inflammation and to exclude an infection (eg, cytomegalovirus [CMV]). (See "Approach to the diagnosis of cytomegalovirus infection".)

  Our practice is to use a pediatric colonoscope and carbon dioxide for insufflating the bowel. If mucosal disease is severe (eg, diffuse ulceration and friability) or looping of the colonoscope is encountered, the extent of the examination is limited to the sigmoid colon. Looping of the colonoscope occurs due to the attachment of the sigmoid and transverse colon to a mobile mesentery, and endoscopic techniques and associated risks are discussed separately. (See "Overview of colonoscopy in adults", section on 'Colonoscope advancement and mucosal inspection'.)

If the endoscopic evaluation is proceeding without difficulty and if the distal mucosal disease is not severe (eg, absence of deep ulcerations), the pediatric colonoscope is advanced beyond the sigmoid colon. (See "Endoscopic diagnosis of inflammatory bowel disease in adults".)

- **Acutely ill, hospitalized patients with severe symptoms** – For hospitalized patients with acute severe colitis, we usually perform a flexible sigmoidoscopy without a bowel preparation to assess the severity of mucosal disease, and we obtain biopsies to exclude infection (eg, CMV). Colonoscopy is generally not required because of the potentially increased risk of perforation especially if the mucosa is severely inflamed [16]. The management of acutely ill patients with UC is discussed separately. (See "Management of the hospitalized adult patient with severe ulcerative colitis".)

INDUCTION OF REMISSION

Goals of therapy — The treatment goal for patients with active UC is to achieve remission (endoscopic and clinical remission) by demonstrating complete mucosal healing. Although the treatment goals for UC are symptomatic improvement (ie, resolution of diarrhea and bleeding) and endoscopic healing, histologic improvement is emerging as an important component of disease remission [2]. Response to therapy can be determined by assessing symptoms, laboratory testing, and supplemented by endoscopy with biopsies as needed. (See 'Monitoring during remission' below.)

Initial treatment of UC is based upon disease severity and extent. (See 'Disease activity, severity, and risk' above.) Most patients with mild to moderate UC respond to 5-aminosalicylic acid (5-ASA) with or without an induction course of oral or topical glucocorticoids. (See 'Ulcerative proctitis or proctosigmoiditis' below and 'Left-sided or extensive colitis' below.)

Ulcerative proctitis or proctosigmoiditis

Initial therapy

Topical mesalamine — We and several society guidelines prefer topical (rectal) mesalamine as first-line treatment for inducing remission in low-risk patients with mild to moderate ulcerative proctitis or proctosigmoiditis (table 1) [1,2].

Mesalamine is widely available in two forms: suppository or enema. Foam and gel preparations of mesalazine (ie, the international generic name) are available in countries outside the United States [17,18]. Enemas reach the proximal sigmoid colon and splenic flexure in most patients

who are able to retain them [19]. By contrast, foam preparations generally reach the midsigmoid colon [20], while suppositories are effective only for disease limited to the rectum (ie, within 18 cm from the anal verge).

Outpatient therapy is appropriate for most patients, and choice of a specific treatment will depend upon the distribution of disease (table 1):

- **Ulcerative proctitis** – For patients with mild to moderate disease confined to the rectum, we begin with mesalamine suppository, 1 gram once daily (algorithm 1) [21,22]. For patients who do not have symptomatic relief after an initial two-week course of mesalamine suppositories, we increase the dose to 1 gram twice daily for two to four weeks. We then reduce the dose of the mesalamine suppository to 1 gram daily.

- **Ulcerative proctosigmoiditis** – For patients with mild to moderate disease extending above 18 cm from anal verge into the sigmoid colon, we begin with mesalamine enemas administered rectally once daily. For patients with fecal urgency and tenesmus, we also begin mesalamine suppository 1 gram once daily. Patients who cannot retain enemas due to rectal irritability may use a mesalamine foam preparation (available in Canada). Rectal glucocorticoid foam preparations are also an option for a short course (two to four weeks) of induction therapy for patients who cannot retain mesalamine enemas. (See 'Alternative therapy' below.)

  For patients without symptomatic relief after two weeks of daily mesalamine enemas, we either increase the mesalamine enema to twice daily or continue once daily enema and add a mesalamine suppository 1 gram once daily, depending on patient preference. Twice daily topical mesalamine dosing is given for four weeks, followed by resuming the once daily mesalamine enema.

Symptomatic improvement (eg, decrease in bleeding and stool frequency) can be expected within one week of initiating topical mesalamine therapy. However, clinical remission usually requires four to six weeks or longer, and we continue topical mesalamine treatment to maintain remission. (See 'Maintenance of remission' below.)

Topical (rectal) mesalamine is effective for inducing remission in patients with mild to moderate proctitis or proctosigmoiditis [23,24]. In a meta-analysis of eight trials including 811 patients, patients treated with rectal mesalamine were more likely to achieve symptomatic remission compared with patients given placebo (pooled odds ratio [OR] 8.3, 95% CI 4.28-16.12) [24].

In addition, topical mesalamine preparations are preferred over oral 5-ASA therapy and over topical (rectal) glucocorticoids [1]:

- In a meta-analysis of three trials including 155 patients with distal UC or proctitis, patients treated with topical mesalamine were less likely to lack clinical improvement compared with patients treated with oral agents (mesalamine 2 to 3 grams daily or sulfasalazine 4 grams daily) (relative risk [RR] 0.28, 95% CI 0.14-0.56) [23,25-27]. Sulfasalazine is a prodrug composed of 5-ASA linked to sulfapyridine through an azo bond (figure 1). (See "Sulfasalazine and 5-aminosalicylates in the treatment of inflammatory bowel disease", section on 'Pharmacology'.)

- In a meta-analysis of six trials, patients with distal UC treated with topical mesalamine were more likely to achieve symptomatic remission compared with those on topical glucocorticoids (OR 1.65, 95% CI 1.11-2.45) [24].

Alternative therapy — Alternative agents are available as initial therapy for patients with a hypersensitivity to topical mesalamine or for patients who are unable or unwilling to use topical therapies in general:

- **Topical glucocorticoids** – Patients who cannot tolerate topical mesalamine but who can use rectal therapy are treated with topical glucocorticoids, and the formulation depends on disease extent (table 1):

  - **Ulcerative proctitis** – If disease is limited to the rectum (≤18 cm from the anal verge), we use a glucocorticoid suppository (ie, hydrocortisone) once daily for two weeks for induction of remission. For patients without symptomatic relief after two weeks, we increase the dosing frequency to twice daily for ≤4 weeks, followed by decreasing the frequency to once daily for ≤2 weeks, and then discontinue it. We limit the duration of use to ≤8 weeks because of the potential for systemic side effects (eg, adrenal suppression) with topical glucocorticoids.

  - **Ulcerative proctosigmoiditis** – If colitis extends beyond 18 cm from the anal verge, we typically use a glucocorticoid foam preparation or glucocorticoid enema once daily [1,28]. For patients without symptomatic relief after two weeks of therapy, glucocorticoid enemas are given twice daily for ≤4 weeks and then decreased to daily use for ≤2 weeks. We limit the duration of topical glucocorticoid use to ≤8 weeks because of the potential for systemic side effects. Alternatively, a twice daily regimen consisting of glucocorticoid suppository in the morning and a glucocorticoid enema (or foam) preparation at bedtime is an alternative to twice daily enemas for patient convenience. The specific regimen of topical glucocorticoids is often based on patient preferences, product availability, insurance coverage/cost, and clinician preference.

(See "Overview of budesonide therapy for adults with inflammatory bowel disease", section on 'Rectal formulations'.)

Symptomatic improvement (eg, decreased bleeding and stool frequency) is usually seen three to four weeks after starting topical glucocorticoid therapy. Long-term use (ie, >8 weeks) is generally avoided because the efficacy has not been established and may be associated with adverse effects of chronic topical glucocorticoid use [29].

- **Oral 5-ASA agents** – Patients who are unwilling or unable to tolerate topical medications can be treated with an oral 5-ASA medication (table 1). We prefer to begin with high-dose mesalamine (ie, >3 grams daily), while sulfasalazine (4 grams daily) is an alternative option especially in patients with inflammatory bowel disease-associated arthritis [30,31]. We prefer using oral mesalamine once daily dosing to optimize patient adherence (similar to society guidelines) [1]. The selection of a specific formulation of mesalamine also depends on insurance coverage/cost, product availability, convenience of dosing, and clinician preference. After remission is achieved (typically within eight weeks), decreasing the mesalamine dose to 2 to 3 grams per day is reasonable, whereas continuing the high dose is acceptable also.

  While we use high-dose mesalamine (ie, >3 grams daily) for induction therapy, some society guidelines prefer either mesalamine at standard dose (ie, 2 to 3 grams daily) or diazo-bonded 5-ASA (eg, balsalazide) [1,2]. The formulations, pharmacology and adverse effects of 5-ASA agents are discussed separately. (See "Sulfasalazine and 5-aminosalicylates in the treatment of inflammatory bowel disease".)

  Oral mesalamine at either a standard (2 to 3 grams daily) or high (>3 grams daily) dose is effective for inducing remission for patients with mild to moderate UC. In a meta-analysis, the risk of failing to achieve remission was lower in patients on either high or standard dose mesalamine compared with patients given placebo (high dose, six trials including 904 patients: RR of failure to achieve remission 0.75, 95% CI 0.66-0.86; standard dose, eight trials including 1199 patients: RR 0.84, 95% CI 0.78-0.91) [23]. In addition, the risk of failing to achieve remission was lower in patients given high-dose or standard-dose mesalamine compared with low-dose mesalamine (<2 grams daily) (high dose, six trials including 519 patients: RR 0.81, 95% CI 0.71-0.92; standard dose, eight trials including 906 patients: RR 0.88, 95% CI 0.79-0.99) [23].

Subsequent therapy — For patients who tolerate topical mesalamine but who do not have improvement in symptoms after four weeks of therapy, subsequent options include (table 1) [26,32]:

- Add a topical glucocorticoid (eg, suppository, enema) once daily to the existing topical mesalamine,
- Add an oral 5-ASA agent to the existing topical mesalamine regimen, or
- Start an oral glucocorticoid (ie, budesonide multimatrix [MMX] or prednisone)

For example, topical therapy is given twice daily (ie, glucocorticoid once daily and mesalamine daily) for patients without symptomatic improvement after four weeks of topical mesalamine alone. If there is no symptomatic improvement after two to four weeks of the topical glucocorticoid/mesalamine regimen, we then add an oral 5-ASA agent while continuing topical therapy. The approach to initiating oral 5-ASA therapy and the efficacy of such therapy is described above. (See 'Alternative therapy' above.)

If there is no improvement after two to four weeks, we start an oral glucocorticoid. Patients who fail to respond to combination therapy with oral 5-ASA agent and topical mesalamine (and/or topical glucocorticoids) require treatment with oral glucocorticoids, as discussed below. (See 'Subsequent therapy' below.)

Left-sided or extensive colitis

Initial therapy — We use a combination of an oral 5-ASA agent plus rectal mesalamine for patients with left-sided or extensive mildly to moderately active UC. Symptomatic improvement is usually seen within two to four weeks.

We prefer to begin high-dose mesalamine (ie, >3 grams daily) as the initial oral therapy for patients with left-sided colitis or extensive colitis; sulfasalazine 4 grams per day is an alternative option [30,31]. Our practice differs from the American Gastroenterological Association guideline that recommends initial oral therapy with either standard dose mesalamine (ie, 2 to 3 grams daily) or diazo-bonded 5-ASA (eg, balsalazide) [1,33]. (See 'Alternative therapy' above.)

Different formulations of oral 5-ASA agents have been developed for site-specific, targeted delivery of 5-ASA. The 5-ASA formulations include mesalamine, sulfasalazine (a prodrug of 5-ASA), and diazo-bonded 5-ASA (table 1). The formulations and adverse effects of 5-ASA agents, including details regarding folate supplementation with sulfasalazine use, are discussed separately. (See "Sulfasalazine and 5-aminosalicylates in the treatment of inflammatory bowel disease".)

For topical therapy, we use mesalamine enemas once daily initially for two months. Deciding whether to continue mesalamine enemas after achieving remission is based on patient preference and tolerance. For patients who cannot retain enemas due to rectal irritability, 5-ASA foam preparations or 5-ASA rectal suppositories are alternatives.

Patients who are given both 5-ASA oral and topical therapy are less likely to fail to achieve remission compared with patients on oral 5-ASA monotherapy [26,34-36]. In a meta-analysis of four trials including 321 patients with left-sided or extensive colitis, combined oral and topical 5-ASA therapy was less likely to fail to induce remission compared with oral 5-ASA (or sulfasalazine) alone (RR 0.68, 95% CI 0.49-0.94) [23].

Subsequent therapy — The following are treatment options for patients who do not respond (ie, minimal to no improvement in symptoms such as diarrhea, rectal bleeding) after two to four weeks of combination therapy consisting of oral 5-ASA agent and rectal mesalamine (table 1):

- **Oral 5-ASA agent plus topical (rectal) glucocorticoids** – For patients who do not respond to combination therapy, topical mesalamine can be replaced with topical glucocorticoid therapy (enema, foam, or suppository daily), while the oral 5-ASA agents are continued.

- Budesonide **multimatrix** – For patients who do not respond to a combination of oral 5-ASA and topical mesalamine (or topical glucocorticoids), budesonide MMX can be added to the existing regimen. We give budesonide MMX at a dose of 9 mg daily for eight weeks and then stop it without a taper [37]. For patients who develop symptoms of relapse (eg, diarrhea, rectal bleeding) at ≥8 weeks after discontinuing budesonide, a second course of budesonide (9 mg daily for eight weeks) is given. If symptoms improve with treatment, we discontinue budesonide without a taper. An alternative approach used by some clinicians for the second budesonide course is to taper budesonide MMX as follows: 9 mg daily for four weeks; then 9 mg every other day for two weeks; and then 9 mg every third day for two weeks (ie, total of eight weeks for the second course of therapy). However, there are no data to support this gradual dose reduction.

  Patients who cannot stop budesonide due to symptom recurrence within eight weeks of discontinuation require escalation of therapy to prednisone (discussed below) or a biologic agent, which is discussed separately. (See "Management of moderate to severe ulcerative colitis in adults", section on 'Induction of remission'.)

  Colonic release budesonide is effective for inducing remission for patients with UC, and budesonide MMX formulation extends its delivery to the entire colon. In a meta-analysis of three trials including 479 patients, budesonide MMX at 9 mg daily for eight weeks was more effective for inducing endoscopic and clinical remission in patients with mild to moderate UC compared with placebo (RR of failure to induce remission 0.88, 95% CI 0.83-0.94) [23,37-39]. Long-term efficacy and safety data for maintaining remission with budesonide MMX are lacking, and thus it is only used as induction therapy.

The use of glucocorticoids with a high first-pass metabolism and lower risk of adverse effects is preferred over systemic glucocorticoids, and the pharmacology, dosing, and safety of budesonide are discussed separately. (See "Overview of budesonide therapy for adults with inflammatory bowel disease".)

- Prednisone – For patients whose symptoms do not improve with budesonide MMX, we discontinue budesonide MMX and initiate systemic glucocorticoid therapy with prednisone. Oral prednisone is started at a dose of 40 mg daily, and we typically begin to taper prednisone after one week of high-dose therapy. However, some clinicians continue high-dose glucocorticoid therapy for up to four weeks prior to initiating a taper. We generally taper prednisone by either 5 mg or 10 mg increments on a weekly basis for a total duration of four to eight weeks of therapy. For patients who have been treated with glucocorticoids for greater than three months, a slower taper may be needed to avoid adrenal insufficiency, and this is discussed separately [40]. (See "Glucocorticoid withdrawal".)

  Prednisone typically results in symptomatic improvement within one week. However, prednisone is not given as long-term therapy because of the risk of adverse effects [41]. Patients are regarded as having steroid-dependent UC if glucocorticoids cannot be tapered to less than 10 mg daily within three months of starting glucocorticoids without recurrence of disease or if relapse occurs within three months of stopping glucocorticoids [42]. Such patients typically require escalation to other therapies for long-term maintenance (eg, biologic agents), and this is discussed separately. (See "Management of moderate to severe ulcerative colitis in adults", section on 'Induction of remission'.)

  Oral glucocorticoids are effective for inducing remission in patients with active UC. In a meta-analysis of three trials including 247 patients, the risk of failing to achieve remission was lower for patients treated with glucocorticoids compared with placebo (RR 0.47, 95% CI 0.24-0.90) [43].

MAINTENANCE OF REMISSION

Goals of and indications for therapy — After clinical remission has been achieved in a patient with mild to moderate UC, the goal of management is to prevent clinical and endoscopic relapse. The following patients generally require maintenance therapy [40]:

- Patients with ulcerative proctitis and >1 disease flare per year
- All patients with ulcerative proctosigmoiditis

- All patients with ulcerative colitis proximal to the sigmoid colon (ie, left-sided colitis and extensive colitis)

Patients with ulcerative proctitis and ≤1 flare per year that responds to topical mesalamine do not require maintenance therapy, because such patients often have long-term remission without a relapse. If a relapse does occur, symptoms typically resolve quickly with topical mesalamine therapy.

Ulcerative proctitis or proctosigmoiditis — The choice of maintenance therapy depends on the specific agent used to induce remission, the distribution of disease, patient preferences, clinician preferences, and insurance coverage/cost. (See 'Ulcerative proctitis or proctosigmoiditis' above.)

For example (table 1):

- For patients with ulcerative proctitis who responded to topical mesalamine for induction of remission and who have >1 flare per year, we use a maintenance regimen of one mesalamine suppository (1 gram) every night.
- For patients with ulcerative proctosigmoiditis who responded to topical mesalamine for induction of remission, we use a maintenance regimen of one mesalamine enema every night.
- For patients who are unwilling to use daily topical therapy for long-term maintenance, we reduce the dosing frequency (eg, suppository or enema given every other day or twice weekly), although there are no published data to support this practice [44].
- For patients who required an oral 5-ASA agent to achieve remission, we continue oral 5-ASA therapy to maintain remission. We generally continue the induction dose of oral 5-ASA (ie, >3 grams daily), although some clinicians reduce the dose to 2 to 3 grams per day). Patients with frequent relapses (ie, ≥2 flares per year) may benefit from a higher dose of maintenance oral 5-ASA therapy (ie, mesalamine >3 grams daily) [45,46]. (See 'Left-sided or extensive colitis' below.)

Topical mesalamine reduces the risk of relapse for patients with UC in remission [47,48]. In a meta-analysis of seven trials including 555 patients with inactive mild to moderate UC (limited to distal colitis in six trials), patients maintained on topical mesalamine were less likely to relapse compared with patients given placebo (relative risk [RR] 0.60, 95% CI 0.49-0.73) [48].

Topical glucocorticoids (ie, suppository, foam or enema) are not used for maintenance therapy because of lack of efficacy data and the risk of adverse effects and complications [49]. (See

"Major side effects of systemic glucocorticoids".)

Left-sided or extensive colitis — The choice of maintenance therapy depends on the specific agent used to induce remission, the distribution of disease, patient preferences, clinician preferences, and insurance coverage/cost. (See 'Left-sided or extensive colitis' above.)

For example, oral 5-ASA agents and/or topical mesalamine formulations are used to maintain remission in patients with left-sided or extensive mild to moderate UC (table 1) [40]:

- **Oral 5-ASA agents** – For patients who achieved remission with high-dose oral mesalamine, the dose may be continued at the induction dosing (>3 grams daily) or decreased to 2 to 3 grams daily, and the choice depends on clinician and patient preference. For patients who achieved remission with standard dose oral mesalamine (2 to 3 grams daily), the dose may be continued at the induction dosing.

  In our experience, a mesalamine dose of 2 to 3 grams daily is efficacious in maintaining remission for most patients; however, reducing the dose to ≤3 grams per day may increase the risk of relapse for some patients. Patients who flare while on maintenance mesalamine doses ≤3 grams often require a dose increase to prevent recurrence after remission is achieved again [45].

  Oral 5-ASA medications are effective in the maintenance of remission in patients with UC [50-55]. In a meta-analysis of 11 randomized trials, the risk of relapse was lower in patients with inactive UC maintained with oral 5-ASA agents as compared with placebo (RR 0.65, 95% CI 0.55-0.76) [55].

- **Topical** mesalamine – We use topical mesalamine as maintenance therapy regimen primarily for patients with left-sided colitis whose symptoms are well controlled with topical therapy [48]. The dosing frequency is once daily for long-term maintenance therapy. (See 'Ulcerative proctitis or proctosigmoiditis' above.)

  We typically do not use long-term topical mesalamine therapy for patients with extensive colitis.

Both systemic (eg, prednisone) and locally acting (eg, budesonide multimatrix) glucocorticoids are not used for maintenance therapy, because of lack of efficacy data and the risk of adverse effects [37,56]. (See "Major side effects of systemic glucocorticoids".)

Monitoring during remission — We assess patients clinically and with colonoscopy in 6 to 12 months after achieving clinical remission because the therapeutic goal is mucosal healing but correlation between clinical symptoms and endoscopic mucosal appearance is limited. In

addition, noninvasive markers of inflammation can be useful. We obtain inflammatory markers including CRP and a fecal biomarker (ie, fecal calprotectin or fecal lactoferrin) at the time of colonoscopy and correlate these tests with the degree of mucosal healing. In some patients with UC, CRP does not correlate with endoscopic findings, and we do not rely solely on CRP for monitoring patients with inactive disease [2].

For patients in remission, we continue to measure noninvasive biomarkers every 6 to 12 months. For patients with abnormal results (ie, calprotectin ≥150 mcg/g, positive lactoferrin, or elevated CRP), we typically perform lower endoscopy to assess endoscopic disease activity and guide adjustments in therapy [3].

We monitor inflammatory biomarkers because elevated biomarkers have been associated with increased risk of disease relapse. In a meta-analysis of 17 studies with 1286 patients with UC in symptomatic remission, elevated fecal calprotectin (defined in most studies as >150 mcg/g) was associated with higher risk of disease relapse compared with patients who had a normal fecal calprotectin level after a median follow-up of one year (risk ratio [RR] 4.36, 95% CI 3.48-5.47) [3].

FAILURE TO RESPOND

Some patients may fail to respond to induction therapy for mild to moderate UC, and such patients are reassessed for disease progression, noncompliance with medical therapy, or an alternative etiology (eg, functional symptoms). (See 'Induction of remission' above and 'Pretreatment evaluation' above.):

- Compliance – Some patients who are noncompliant with topical therapy report difficulty with administration and retention of enemas due to rectal irritation [57]. Such patients can be treated with a topical glucocorticoid foam preparation rather than a mesalamine enema. (See 'Ulcerative proctitis or proctosigmoiditis' above.)

- Refractory disease – Patients who do not have symptomatic improvement with systemic glucocorticoids (eg, prednisone 40 mg per day) within one to two weeks of initiating therapy are regarded as having glucocorticoid-refractory disease. Treatment options include a biologic agent (eg, anti-tumor necrosis factor agent) or a small molecule (tofacitinib). The management of patients with steroid-refractory UC is discussed in detail separately. (See "Management of moderate to severe ulcerative colitis in adults", section on 'Intravenous glucocorticoids'.)

OTHER THERAPIES

- Antidiarrheal medications – A short course of symptomatic treatment (7 to 10 days) is an option for patients with mild to moderate UC and no signs of systemic toxicity (eg, fever or tachycardia) who are not responding to therapy with anti-inflammatory medications. For patients who have mild intermittent diarrhea without signs of systemic toxicity, we use loperamide as needed in small doses (ie, 2 to 4 mg after an episode of loose stool) for management of diarrhea in this setting because of its efficacy and safety in low doses [58]. An alternative to loperamide is a bile acid sequestrant as needed for mild diarrhea (eg, cholestyramine), and this is discussed separately. (See "Microscopic (lymphocytic and collagenous) colitis: Clinical manifestations, diagnosis, and management", section on 'Cholestyramine'.)

- Medications to avoid – Opioids should be avoided because they can mask the signs and symptoms of an acute abdomen or increase the risk of developing toxic megacolon, and because of their addiction potential. (See "Toxic megacolon".)

  Although there are limited data, nonsteroidal anti-inflammatory drugs should be avoided due to their potential to exacerbate inflammatory bowel disease [59,60].

NUTRITION

Nutrition and dietary therapy for patients with inflammatory bowel disease is discussed separately. (See "Nutrition and dietary management for adults with inflammatory bowel disease".)

HEALTH MAINTENANCE

It is important to perform routine health maintenance, including screening for and prevention of other diseases as well as monitoring for adverse effects of therapy in patients with inflammatory bowel disease (IBD) [61]. The Crohn's and Colitis Foundation provides a health maintenance checklist for adult patients with IBD [62].

Approach to vaccination — As part of our initial evaluation of patients with IBD, we review each patient's vaccination and exposure history [61]. Ideally, this review should be performed before the start of immunosuppressive therapy, when the likelihood of developing a protective immune response to any needed vaccine is highest and when live vaccines can be given safely. In general, patients with IBD require the following inactivated (nonlive) vaccines (figure 2) [63]:

- Seasonal nonlive influenza vaccine (annually)
- Pneumococcal vaccine (for patients who are on or are planning to start immunosuppressive therapy)

In addition, patients are screened for hepatitis B virus before initiating biologic or immunosuppressive therapy, and individuals who are seronegative should be vaccinated for hepatitis B virus [64]. (See "Hepatitis B virus immunization in adults".)

Patients who are not up to date with other routinely recommended vaccines (based on age or other risk factors) should receive any needed inactivated (nonlive) vaccines regardless of immunosuppression. Any needed live vaccines (eg, measles vaccine) should ideally be administered ≥4 weeks prior to the start of immunosuppression. The approach to immunizations for patients with IBD is similar to the care of patients with autoimmune inflammatory rheumatic conditions, and this is discussed in more detail separately. (See "Immunizations in autoimmune inflammatory rheumatic disease in adults".)

Immunization recommendations in the United States result from policies developed by the Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention [65]. This is discussed separately. (See "Standard immunizations for nonpregnant adults", section on 'Immunization schedule for nonpregnant adults'.)

Patients with IBD are at increased risk for infections due to their underlying disease, malnutrition, surgery, and/or immunosuppressive medications [66-68].

Cancer screening

- **Colorectal cancer** – Patients with IBD are at increased risk for colorectal cancer (CRC) and should undergo CRC screening with colonoscopy based on the extent and duration of their disease [69]. (See "Surveillance and management of dysplasia in patients with inflammatory bowel disease".)

- **Cervical cancer** – Annual screening for cervical cancer should be performed for women with IBD on immunosuppressive therapy [61]. It is important for clinicians to emphasize the importance of cervical cancer screening for women with IBD on immunosuppressive therapy; compliance with cervical cancer screening tends to be low in women with IBD [70,71]. (See "Screening for cervical cancer in patients with HIV infection and other immunocompromised states", section on 'Immunosuppressed patients without HIV'.)

- **Skin cancer** – All IBD patients who have taken, are currently taking, or are planning to start immunomodulators or biologic therapy should undergo annual skin examination by

a dermatologist [61,72]. Both melanoma and nonmelanoma skin malignancies are associated with therapies used for IBD. Nonmelanoma skin cancer is associated with past or current use of 6-mercaptopurine or azathioprine. Patients should be advised to avoid excessive sun exposure and use a high-strength sunscreen and sun-protective measures [61]. (See "Dermatologic and ocular manifestations of inflammatory bowel disease", section on 'Rare dermatologic diseases' and "Selection of sunscreen and sun-protective measures", section on 'Selection of sunscreen products'.)

Osteoporosis screening — Patients with IBD are at increased risk for bone loss [73]. Screening for osteoporosis with bone mineral density testing should be performed at the time of diagnosis and periodically thereafter in all IBD patients who meet one of the following criteria: postmenopausal, ongoing glucocorticoid treatment, cumulative prior use of glucocorticoids exceeding three months, history of low-trauma fractures, or age over 60 years [61]. The frequency is determined by established guidelines for the general population. (See "Screening for osteoporosis in postmenopausal women and men".)

IBD patients on glucocorticoids (any dose with an anticipated duration of ≥3 months) should maintain a total calcium intake of 1200 mg per day and vitamin D intake of 800 international units per day through either diet and/or supplements. Treatment with bisphosphonates for patients with IBD is discussed separately. (See "Metabolic bone disease in inflammatory bowel disease".)

Anxiety/depression screening — Many IBD patients suffer from anxiety and depression secondary to their disease and should be screened for these conditions [74-76]. (See "Screening for depression in adults", section on 'Screening instruments'.)

Laboratory monitoring — Periodic laboratory monitoring is necessary to detect complications associated with IBD and side effects of medical therapy.

- **Anemia** – Approximately 35 to 90 percent of adults with IBD are iron deficient. Other potential causes of anemia in patients with IBD include anemia of chronic disease, vitamin B12 deficiency, folic acid deficiency, or drug-induced anemia (eg, patients treated with sulfasalazine or thiopurines). (See "Vitamin and mineral deficiencies in inflammatory bowel disease".)

  In patients with IBD, complete blood count (CBC) should be measured every 6 to 12 months. In patients with anemia or those with low MCV, we also check ferritin, transferrin saturation, and CRP. The CRP is important in the interpretation of the ferritin level, as ferritin is an acute phase reactant. The diagnosis of iron deficiency is discussed in more

detail separately. (See "Causes and diagnosis of iron deficiency and iron deficiency anemia in adults".)

- **Side effects of therapy** – For patients on 5-ASA agents, we measure serum creatinine at six weeks, three months, six months, and 12 months after initiation of therapy and then annually [77]. (See "Sulfasalazine and 5-aminosalicylates in the treatment of inflammatory bowel disease".)

  For patients who are initiated on 6-mercaptopurine or azathioprine, laboratory monitoring (ie, hemoglobin, white blood cell count, platelet count, liver blood tests [serum aminotransferases and total bilirubin]) is performed at short intervals (eg, weekly or every other week) until a maintenance dose is reached. Laboratory testing is continued periodically for the duration of therapy, and the specific monitoring schedules are discussed separately. (See "Overview of azathioprine and mercaptopurine use in inflammatory bowel disease", section on 'Dosing and monitoring'.)

- **Disease activity** – The stool marker, calprotectin, may be used to monitor disease activity in patients with IBD. A systematic review of six studies of 552 IBD (mostly UC) patients in remission showed that ≥2 elevated calprotectin measurements corresponded to a 53 to 83 percent probability of relapse within the next two to three months [78]. (See 'Monitoring during remission' above.)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Ulcerative colitis in adults".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient education: Ulcerative colitis in adults (The Basics)")
- Beyond the Basics topics (see "Patient education: Ulcerative colitis (Beyond the Basics)" and "Patient education: Sulfasalazine and the 5-aminosalicylates (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- **Defining disease severity and risk** – Patients with mild to moderate ulcerative colitis (UC) are identified as low risk based on prognostic factors that suggest a nonaggressive form of disease: absence of deep mucosal ulcerations, no extraintestinal manifestations, and diagnosis at age >40 years. These patients usually have mild to moderate symptoms (≤6 stools daily with or without blood) and lack signs of systemic inflammation (ie, normal or minimal elevation in C-reactive protein and/or fecal calprotectin levels). (See 'Disease activity, severity, and risk' above.)
- **Pretreatment evaluation** – For patients with UC who present with symptoms of a disease flare (eg, diarrhea, rectal bleeding), some aspects of the initial evaluation (eg, laboratory and stool studies, lower endoscopy) are repeated to exclude other conditions as a cause for symptoms and to assess the extent and severity of disease. (See 'Pretreatment evaluation' above.)
- **Goals of therapy** – The treatment goal for patients with active UC is to achieve clinical and endoscopic remission by demonstrating complete mucosal healing. Response to therapy can be determined by assessing symptoms and laboratory testing and can be supplemented by endoscopy with biopsies as needed. (See 'Goals of therapy' above.)
- **Induction therapy for ulcerative proctitis or proctosigmoiditis** – For low-risk patients with ulcerative proctitis or proctosigmoiditis, we suggest topical (rectal) mesalamine rather than oral mesalamine or observation (table 1) (**Grade 2B**). However, for patients who prefer to avoid the burden of daily topical treatment, it is also reasonable to use oral mesalamine or to observe and initiate treatments if disease progresses. (See 'Initial therapy' above.)

  For patients with mild to moderate disease confined to the rectum, we typically initiate treatment with mesalamine suppository once daily (algorithm 1). For patients with mild

to moderate disease extending above 18 cm from anal verge into the sigmoid colon, we treat with mesalamine enema once or twice daily.

For low-risk patients with ulcerative proctitis or proctosigmoiditis who do not have symptom improvement after four weeks of topical mesalamine therapy, subsequent options include adding a topical glucocorticoid (eg, suppository, enema), adding an oral 5-aminosalicylic acid (5-ASA) agent, and/or starting an oral glucocorticoid (eg, budesonide multimatrix). Selection of second-line therapy depends on patient preferences, product availability, clinician preferences, and prior response to therapy. (See 'Subsequent therapy' above.)

- **Induction therapy for left-sided or extensive UC** – For low-risk patients with left-sided or extensive mild to moderate UC, we suggest a combination of an oral 5-ASA agent plus rectal mesalamine for induction therapy rather than oral 5-ASA monotherapy (**Grade 2B**). We begin high-dose oral mesalamine (ie, >3 grams daily) and mesalamine enemas once daily (table 1). (See 'Left-sided or extensive colitis' above.)

- **Maintenance therapy** – We suggest long-term maintenance therapy for the following low-risk patients who have achieved clinical remission with medical therapy (see 'Maintenance of remission' above) (**Grade 2B**):

  - Patients with ulcerative proctitis and >1 disease flare per year
  - Patients with ulcerative proctosigmoiditis
  - Patients with UC proximal to the sigmoid colon (ie, left-sided colitis and extensive colitis)

  The choice of maintenance therapy depends on the specific agent used to induce remission, the distribution of disease, patient preferences, clinician preferences, and insurance coverage/cost. For low-risk patients with mild to moderate UC in remission, the goal of management is to prevent clinical and endoscopic relapse.

- **Health maintenance** – Routine health maintenance, including screening for and prevention of other diseases as well as monitoring for adverse effects of therapy, is an important aspect of the care of patients with inflammatory bowel disease. (See 'Health maintenance' above.)

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GRAPHICS

Medical therapy for mild to moderate ulcerative colitis

Role	Medication	Brand name (United States or as noted)	Usual dose
Induction of remission	**Topical (rectal) mesalamine***		
	Suppository	Canasa, Mezera¶, Pentasa¶, Salofalk¶	1 gram (one suppository) once daily at bedtime
	Retention enema	Pentasa¶, Rowasa, Salofalk¶	4 grams once daily at bedtime or twice daily$^{\Delta}$
	Rectal foam (United States: Not available)	Mezera¶	2 grams (two actuations) once daily at bedtime
	Topical (rectal) glucocorticoids		
	Hydrocortisone suppository	Anucort-HC, Anusol-HC, Hemmorex-HC, Proctocort	One suppository (25 or 30 mg) once or twice daily
	Hydrocortisone aerosol foam 10%	Cortifoam	90 mg (one applicatorful) once or twice daily
	Hydrocortisone enema	Cortenema, Colocort	100 mg (one 60 mL unit) once or twice daily
	Budesonide aerosol foam	Uceris	2 mg (one metered dose) once or twice daily
	Budesonide enema (reconstituted dispersible tablets)	Entocort¶	2 mg (one enema) once daily prior to bedtime
	Oral 5-aminosalycylic acid (5-ASA) derivatives		
	Sulfasalazine tablet	Azulfidine, Salazopyrin¶	4 grams per day in four divided doses
	Mesalamine*◇		
	▪ Delayed release enteric coated tablet	Asacol¶, Asacol HD	2.4 to 4.8 grams daily in three divided doses
		Mezera¶	3 grams daily in three divided doses
		Octasa¶	4.8 grams daily or in divided doses

		Salofalk[¶]	3 to 4 grams daily in three to four divided doses
	▪ Capsule containing delayed release enteric coated tablet	Delzicol	2.4 grams daily in three divided doses
	▪ Delayed and extended release tablet, multimatrix (MMX)	Lialda, Mezavant[¶]	2.4 to 4.8 grams daily once daily
	▪ Capsule containing delayed release enteric coated granules	Apriso	1.5 to 4.5 grams once each morning
	▪ Controlled release capsule	Pentasa	4 grams daily in four divided doses
	▪ Mesalamine granules (United States and Canada: Not available)	Salofalk sachet[¶]	1.5 to 3 grams daily in one to three divided doses
		Pentasa sachet[¶]	2 to 4 grams daily in two to four divided doses
	Olsalazine capsule	Dipentum	2 to 3 grams daily in two to four divided doses
	Balsalazide capsule	Colazal	6.75 grams daily in three divided doses
	Oral glucocorticoids		
	Budesonide delayed and extended release tablet, multimatrix (MMX)	Uceris	9 mg once daily in the morning for eight weeks
	Prednisone or prednisolone		40 to 60 mg once daily in the morning or in two divided doses
Maintenance of remission	**Topical (rectal) mesalamine***		
	Suppository	Canasa, Mezera[¶], Pentasa[¶], Salofalk[¶]	1 gram (one suppository) once daily at bedtime

Enema	Pentasa[¶], Rowasa, Salofalk[¶]	1 to 4 grams once daily at bedtime[Δ]
Oral 5-aminosalycylic acid (5-ASA) derivatives		
Sulfasalazine tablet	Azulfidine, Salazopyrin[¶]	2 to 4 grams daily in three or four divided doses
Mesalamine*[◇]		
▪ Delayed release enteric coated tablet	Asacol[¶], Asacol HD	1.6 to 2.4 grams daily in one to three divided doses
▪ Capsule containing delayed release enteric coated tablet	Delzicol	1.6 to 2.4 grams daily in one to three divided doses
▪ Delayed and extended release tablet, multimatrix (MMX)	Lialda, Mezavant[¶]	2.4 to 3.6 grams once daily
▪ Capsule containing delayed release enteric coated granules	Apriso	1.5 to 3 grams once each morning
▪ Controlled release capsule	Pentasa	1.5 to 4 grams daily in three to four divided doses
▪ Mesalamine granules (United States and Canada: Not available)	Salofalk sachet[¶]	1.5 to 4 grams daily in one to three divided doses
	Pentasa sachet[¶]	2 to 4 grams once daily
Olsalazine capsule	Dipentum	1 gram daily in two divided doses
Balsalazide capsule	Colazal	2.25 to 6.75 grams daily in three divided doses

Choice of medication is based on factors including disease location, patient preference and tolerance, and medication availability; refer to UpToDate topic. Approved uses vary by drug,

formulation, and country. Refer to product-specific labeling for more detail. Generic (nonproprietary) products may also be available.

5-ASA: 5-aminosalicylate.

* Mesalamine is a United States generic name. Mesalazine is an international generic (nonproprietary) name.

¶ Not available in the United States; however, is available in other areas (eg, Canada, United Kingdom, Europe).

Δ In the United States, mesalamine enema is available as 4 g/60 mL. Other concentrations and dosages are available elsewhere. Refer to product-specific information.

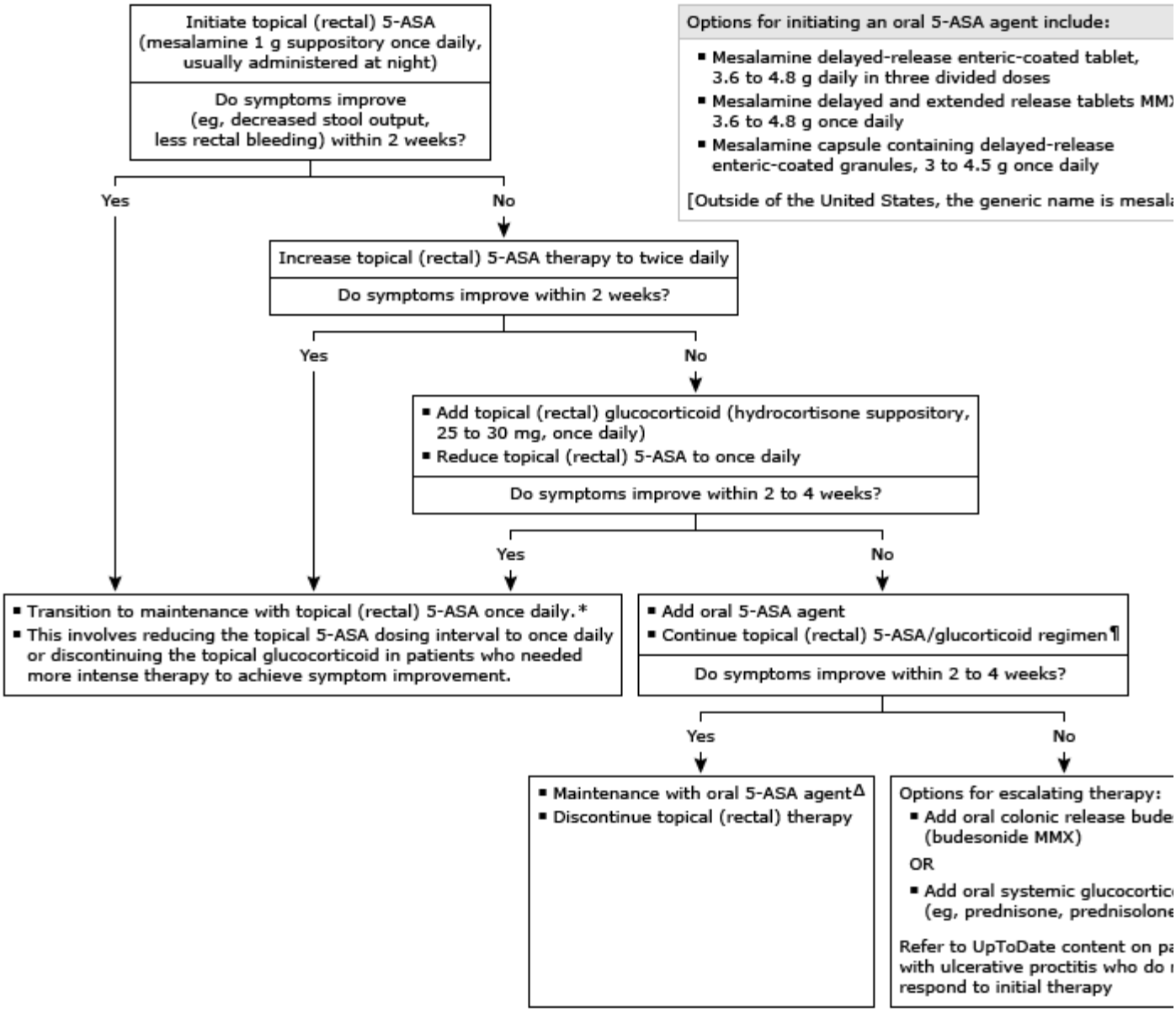
◇ Oral mesalamine may be dosed once daily instead of multiple times daily; there is no significant difference in efficacy and safety.[1,2]

Data courtesy of authors with additional data from:

1. *Ko CW, Singh S, Feuerstein JD, et al. American Gastroenterological Association Institute Clinical Guidelines Committee. AGA clinical practice guidelines on the management of mild-to-moderate ulcerative colitis. Gastroenterology 2019; 156:748.*
2. *Rubin DT, Ananthakrishnan AN, Siegel CA, Sauer BG, Long MD. ACG clinical guideline: Ulcerative colitis in adults. Am J Gastroenterol 2019; 114:384.*
3. *Lexicomp Online. Copyright © 1978-2023 Lexicomp, Inc. All Rights Reserved.*

Graphic 86774 Version 17.0

Approach to the initial management of mild to moderate ulcerative proctitis in



This algorithm represents our approach to managing ulcerative proctitis in adults, but other approaches are reasonable. For example, some clinicians prefer to begin oral 5-ASA agents if topical (rectal) 5-ASA therapy d not result in improvement in symptoms rather than first adding topical (rectal) glucocorticoid therapy. Refer UpToDate content on management of adults with ulcerative colitis for additional details.

5-ASA: 5-aminosalicylic acid; MMX: multi-matrix.

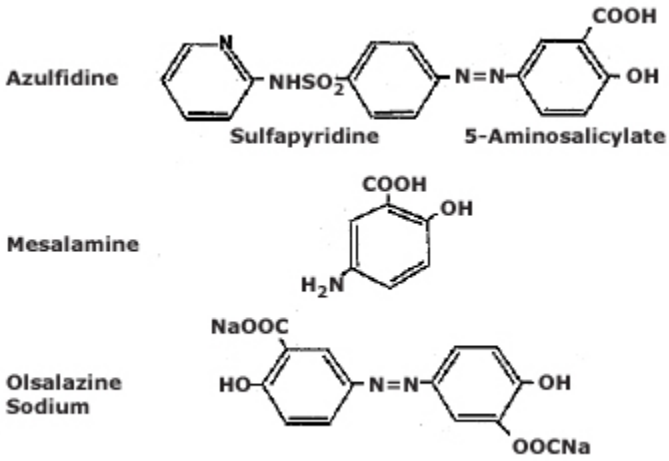
* Patients with ulcerative proctitis who responded to topical (rectal) mesalamine and who have ≤1 flare per do not need maintenance therapy. For patients who responded to topical (rectal) mesalamine and who have flare per year, we use a maintenance regimen of mesalamine suppository once daily. For patients who are unwilling to use daily topical 5-ASA therapy for long-term maintenance, we reduce the dosing frequency (eg suppository every other day or twice weekly).

¶ Use of topical (rectal) glucocorticoids is not generally continued for >8 weeks because of the risk of system adverse effects.

Δ After remission is achieved with an oral 5-ASA agent, the initial dose may be continued (ie, >3 g daily), whe decreasing the dose to 2 to 3 g daily is also a reasonable option.

Graphic 138644 Version 3.0

Structures of sulfasalazine, mesalamine, and olsalazine

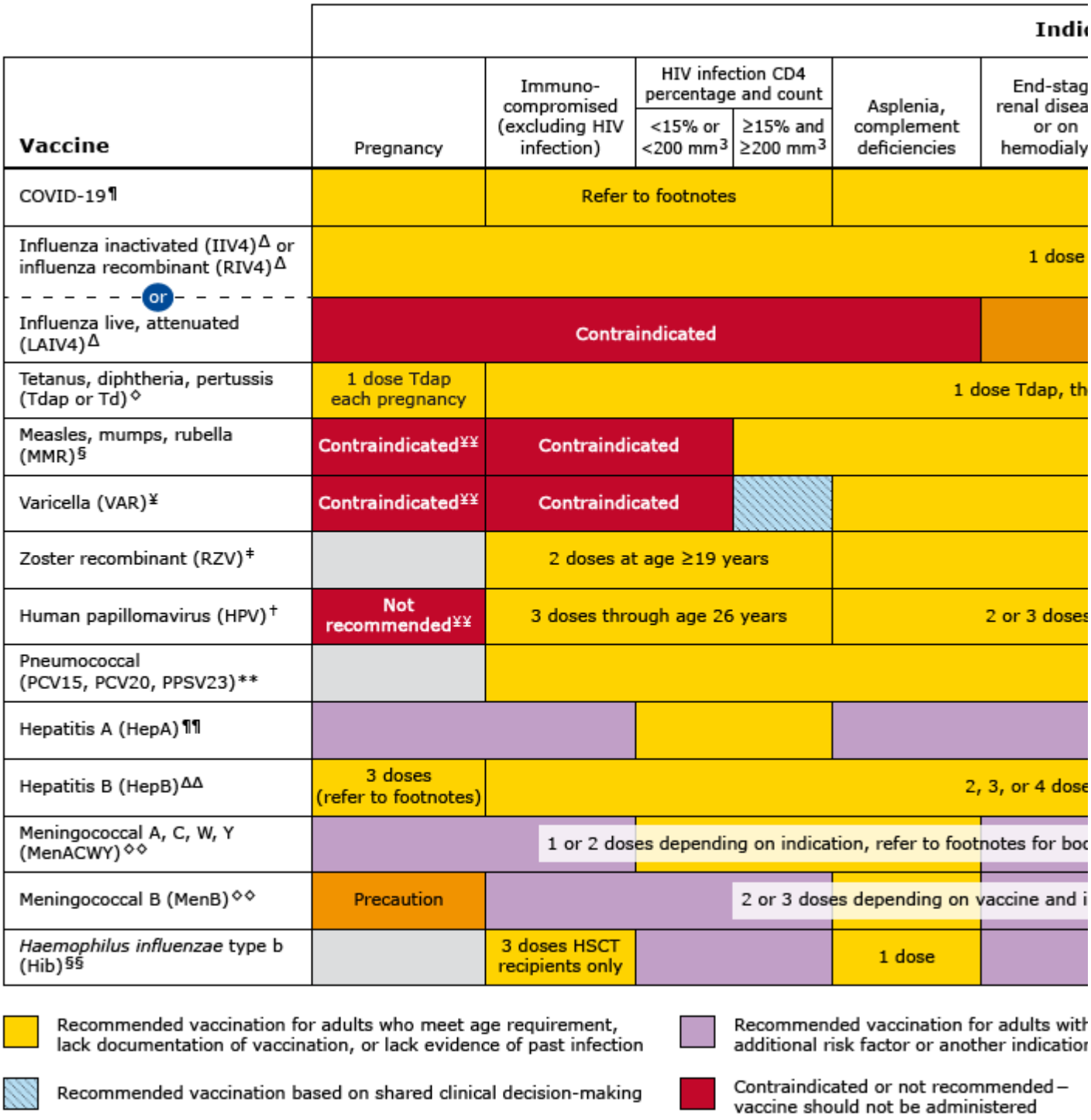


Sulfasalazine is a composite molecule composed of 5-ASA linked by an azo bond to sulfapyridine. Mesalamine is the 5-ASA moiety alone, while olsalazine consists of two 5-ASA molecules joined by an azo bond.

5-ASA: 5-aminosalicylic acid.

Graphic 76617 Version 2.0

Recommended adult immunization schedule by medical condition and other in



Administer recommended vaccines if vaccination history is incomplete or unknown. Do not restart or add do use of trade names is for identification purposes only and does not imply endorsement by the ACIP or CDC.

Polio vaccination

- **Routine vaccination:**
  - Routine poliovirus vaccination of adults residing in the United States is not necessary.
- **Special situations:**

- **Adults at increased risk of exposure to poliovirus with:**
  - **No evidence of a complete polio vaccination series (ie, at least 3 doses):** Administer remain
  - **Evidence of completed polio vaccination series (ie, at least 3 doses):** May administer one life
- For detailed information, refer to www.cdc.gov/vaccines/vpd/polio/hcp/recommendations.html.

HSCT: hematopoietic stem cell transplant.

* Precaution for LAIV4 does not apply to alcoholism.

¶ COVID-19 vaccination

- **Routine vaccination:**
  - **Primary series:** 2-dose series at 0, 4 to 8 weeks (Moderna) or 2-dose series at 0, 3 to 8 weeks (Nov
  - **Booster dose:** Refer to www.cdc.gov/vaccines/covid-19/clinical-considerations/interim-considerati
- **Special situations:**
  - **Persons who are moderately or severely immunocompromised**.
    - **Primary series:**
      - 3-dose series at 0, 4, 8 weeks (Moderna) or 3-dose series at 0, 3, 7 weeks (Pfizer-BioNTech).
      - 2-dose series at 0, 3 weeks (Novavax).
    - **Booster dose:** Refer to www.cdc.gov/vaccines/covid-19/clinical-considerations/interim-conside
    - **Pre-exposure prophylaxis (eg, monoclonal antibodies)** may be considered to complement C considerations/interim-considerations-us.html#immunocompromised.
  - **For Janssen COVID-19 Vaccine recipients** refer to COVID-19 schedule at www.cdc.gov/vaccines/c
  - **NOTE:** Current COVID-19 schedule available at www.cdc.gov/vaccines/covid-19/downloads/COVID- information on Emergency Use Authorization (EUA) indications for COVID-19 vaccines, please visit disease-2019-covid-19/covid-19-vaccines.
- **Contraindications and precautions:**
  - Refer to contraindications and precautions to COVID-19 vaccination.

Δ Influenza vaccination

- **Routine vaccination:**
  - **Age 19 years or older:** 1 dose any influenza vaccine appropriate for age and health status annual
  - **Age 65 years or older:** Any one of quadrivalent high-dose inactivated influenza vaccine (HD-IIV4), adjuvanted inactivated influenza vaccine (aIIV4) is preferred. If none of these three vaccines is ava
  - For the 2022–2023 season, refer to www.cdc.gov/mmwr/volumes/71/rr/rr7101a1.htm.
  - For the 2023–2024 season, refer to the 2023–2024 ACIP influenza vaccine recommendations.
- **Special situations:**
  - **Egg allergy, hives only:** Any influenza vaccine appropriate for age and health status annually.
  - **Egg allergy–any symptom other than hives** (eg, angioedema, respiratory distress, or required e vaccine appropriate for age and health status may be administered. If using egg-based IIV4 or LA provider who can recognize and manage severe allergic reactions.
  - **Close contacts (eg, caregivers, health care workers) of severely immunosuppressed persons** receive LAIV4. If LAIV4 is given, they should avoid contact with/caring for such immunosuppresse
  - **Severe allergic reaction (eg, anaphylaxis) to a vaccine component or a previous dose of any i** precautions.
  - **History of Guillain-Barré syndrome within 6 weeks after previous dose of influenza vaccine:** risks for those at higher risk for severe complications from influenza.
- **Contraindications and precautions:**
  - For contraindications and precautions to influenza vaccination, refer to IIV4 Appendix, LAIV4 Appe

◇ **Tetanus, diphtheria, and pertussis (Tdap) vaccination**

- **Routine vaccination:**
  - **Previously did not receive Tdap at or after age 11 years:** 1 dose Tdap, then Td or Tdap every 10
- **Special situations:**
  - **Previously did not receive primary vaccination series for tetanus, diphtheria, or pertussis:** 1 dose of Td or Tdap 6 to 12 months later (Tdap can be substituted for any Td dose, but preferred as
  - **Pregnancy:** 1 dose Tdap during each pregnancy, preferably in early part of gestational weeks 27 t
  - **Wound management:** Persons with 3 or more doses of tetanus-toxoid-containing vaccine: For cle last dose of tetanus-toxoid-containing vaccine; for all other wounds, administer Tdap or Td if more preferred for persons who have not previously received Tdap or whose Tdap history is unknown. I use Tdap. For detailed information, refer to www.cdc.gov/mmwr/volumes/69/wr/mm6903a5.htm.
- **Contraindications and precautions:**
  - For contraindications and precautions to tetanus, diphtheria, and acellular pertussis (Tdap), refer t

§ **Measles, mumps, and rubella vaccination**

- **Routine vaccination:**
  - **No evidence of immunity to measles, mumps, or rubella:** 1 dose.
    - **Evidence of immunity:** Born before 1957 (health care personnel, refer below), documentatior (diagnosis of disease without laboratory confirmation is not evidence of immunity).
- **Special situations:**
  - **Pregnancy with no evidence of immunity to rubella:** MMR contraindicated during pregnancy; a
  - **Nonpregnant women of childbearing age with no evidence of immunity to rubella:** 1 dose.
  - **HIV infection with CD4 percentages ≥15% and CD4 count ≥200 cells/mm^3 for at least 6 mon** dose series at least 4 weeks apart; MMR contraindicated for HIV infection with CD4 percentage <1
  - **Severe immunocompromising conditions:** MMR contraindicated.
  - **Students in postsecondary educational institutions, international travelers, and household evidence of immunity to measles, mumps, or rubella:** 2-dose series at least 4 weeks apart if pr 1 dose MMR.
  - **In mumps outbreak settings**, for information about additional doses of MMR (including 3rd dos
  - **Health care personnel:**
    - **Born before 1957 with no evidence of immunity to measles, mumps, or rubella:** Consider rubella.
    - **Born in 1957 or later with no evidence of immunity to measles, mumps, or rubella:** 2-dos rubella.
- **Contraindications and precautions:**
  - For contraindications and precautions to measles, mumps, rubella (MMR), refer to MMR Appendix

¥ **Varicella vaccination**

- **Routine vaccination:**
  - **No evidence of immunity to varicella:** 2-dose series 4 to 8 weeks apart if previously did not rece varicella vaccine] for children); if previously received 1 dose varicella-containing vaccine, 1 dose at
    - **Evidence of immunity:** US-born before 1980 (except for pregnant women and health care per vaccine at least 4 weeks apart, diagnosis or verification of history of varicella or herpes zoster
- **Special situations:**
  - **Pregnancy with no evidence of immunity to varicella:** VAR contraindicated during pregnancy; a previously received 1 dose varicella-containing vaccine or dose 1 of 2-dose series (dose 2: 4 to 8 w regardless of whether US-born before 1980.

- **Health care personnel with no evidence of immunity to varicella:** 1 dose if previously received previously did not receive any varicella-containing vaccine, regardless of whether US-born before
- **HIV infection with CD4 percentages ≥15% and CD4 count ≥200 cells/mm^3 with no evidence** VAR contraindicated for HIV infection with CD4 percentage <15% or CD4 count <200 cells/mm^3.
- **Severe immunocompromising conditions:** VAR contraindicated.

▪ **Contraindications and precautions:**

- For contraindications and precautions to varicella (VAR), refer to VAR Appendix.

‡ **Zoster vaccination**

▪ **Routine vaccination:**

- **Age 50 years or older** (NOTE: Serologic evidence of prior varicella is not necessary for zoster vacc available, providers should follow ACIP guidelines for varicella vaccination first. RZV is not indicate RZV in persons without a history of varicella or varicella vaccination)**:** 2-dose series recombinant zo weeks; repeat dose if administered too soon), regardless of previous herpes zoster or history of zo

▪ **Special situations:**

- **Pregnancy:** There is currently no ACIP recommendation for RZV use in pregnancy. Consider delay
- **Immunocompromising conditions** (including persons with HIV regardless of CD4 count; NOTE: I herpes zoster, providers should refer to the clinical considerations for use of RZV in immunocomp recommendations for further guidance: www.cdc.gov/mmwr/volumes/71/wr/mm7103a2.htm)**:** 2-((minimum interval: 4 weeks; repeat dose if administered too soon). For detailed information, refer

▪ **Contraindications and precautions:**

- For contraindications and precautions to zoster recombinant vaccine (RZV), refer to RZV Appendix

† **Human papillomavirus vaccination**

▪ **Routine vaccination:**

- **HPV vaccination recommended for all persons through age 26 years:** 2- or 3-dose series depe
  - **Age 15 years or older at initial vaccination:** 3-dose series at 0, 1 to 2 months, 6 months (min dose 1 to dose 3: 5 months; repeat dose if administered too soon).
  - **Age 9 to 14 years at initial vaccination and received 1 dose or 2 doses less than 5 months**
  - **Age 9 to 14 years at initial vaccination and received 2 doses at least 5 months apart:** HPV
- **Interrupted schedules:** If vaccination schedule is interrupted, the series does not need to be rest
- **No additional dose recommended when any HPV vaccine series has been completed using th**

▪ **Shared clinical decision-making:**

- **Some adults age 27 to 45 years:** Based on shared clinical decision-making, 2- or 3-dose series as

▪ **Special situations:**

- **Age ranges recommended above for routine and catch-up vaccination or shared clinical deci**
  - **Immunocompromising conditions, including HIV infection:** 3-dose series, even for those w
  - **Pregnancy:** Pregnancy testing is not needed before vaccination; HPV vaccination is not recom vaccinated while pregnant.

▪ **Contraindications and precautions:**

- For contraindications and precautions to human papillomavirus (HPV) vaccination, refer to HPV Ap

** **Pneumococcal vaccination**

▪ **Routine vaccination:**

- **Age 65 years or older who have:**
  - **Not previously received a dose of PCV13, PCV15, or PCV20 or whose previous vaccinatior** this should be followed by a dose of PPSV23 given at least 1 year after the PCV15 dose. A min for adults with an immunocompromising condition (NOTE: Immunocompromising conditions

iatrogenic immunosuppression, generalized malignancy, human immunodeficiency virus, Ho transplants, congenital or acquired asplenia, sickle cell disease, or other hemoglobinopathies invasive pneumococcal disease caused by serotypes unique to PPSV23 in these vulnerable gr

- **Previously received only PCV7:** Follow the recommendation above.
- **Previously received only PCV13:** 1 dose PCV20 at least 1 year after the PCV13 dose OR comp www.cdc.gov/vaccines/vpd/pneumo/downloads/pneumo-vaccine-timing.pdf.
- **Previously received only PPSV23:** 1 dose PCV15 OR 1 dose PCV20 at least 1 year after the PP PPSV23.
- **Previously received both PCV13 and PPSV23 but NO PPSV23 was received at age 65 years** vaccine dose OR complete the recommended PPSV23 series as described here: www.cdc.gov/
- **Previously received both PCV13 and PPSV23, AND PPSV23 was received at age 65 years o** least 5 years after the last pneumococcal vaccine dose.
- For guidance on determining which pneumococcal vaccines a patient needs and when, pleas www.cdc.gov/vaccines/vpd/pneumo/hcp/pneumoapp.html.

- **Special situations:**
  - **Age 19 to 64 years with certain underlying medical conditions or other risk factors who hav** alcoholism, chronic heart/liver/lung disease, chronic renal failure, cigarette smoking, cochlear im generalized malignancy, HIV, Hodgkin disease, immunodeficiency, iatrogenic immunosuppressio organ transplants, or sickle cell disease, or other hemoglobinopathies**):**
    - **Not previously received a PCV13, PCV15, or PCV20 or whose previous vaccination history** should be followed by a dose of PPSV23 given at least 1 year after the PCV15 dose. A minimu adults with an immunocompromising condition(NOTE: Immunocompromising conditions inc iatrogenic immunosuppression, generalized malignancy, human immunodeficiency virus, Ho transplants, congenital or acquired asplenia, sickle cell disease, or other hemoglobinopathies
    - **Previously received only PCV7:** Follow the recommendation above.
    - **Previously received only PCV13:** 1 dose PCV20 at least 1 year after the PCV13 dose OR comp www.cdc.gov/vaccines/vpd/pneumo/downloads/pneumo-vaccine-timing.pdf.
    - **Previously received only PPSV23:** 1 dose PCV15 OR 1 dose PCV20 at least 1 year after the PP PPSV23.
    - **Previously received both PCV13 and PPSV23 but have not completed the recommended** dose OR complete the recommended PPSV23 series as described here: www.cdc.gov/vaccines
  - For guidance on determining which pneumococcal vaccines a patient needs and when, please re www.cdc.gov/vaccines/vpd/pneumo/hcp/pneumoapp.html.
- **Contraindications and precautions:**
  - For contraindications and precautions to Pneumococcal conjugate (PCV15 and PCV20), refer to P PPSV23 Appendix.

¶¶ Hepatitis A vaccination

- **Routine vaccination:**
  - **Not at risk but want protection from hepatitis A (identification of risk factor not required):** apart [minimum interval: 6 months]) or 3-dose series HepA-HepB (Twinrix at 0, 1, 6 months [mini
- **Special situations:**
  - **At risk for hepatitis A virus infection:** 2-dose series HepA or 3-dose series HepA-HepB as above
    - **Chronic liver disease** (eg, persons with hepatitis B, hepatitis C, cirrhosis, fatty liver disease, a [ALT] or aspartate aminotransferase [AST] level greater than twice the upper limit of normal).
    - **HIV infection**.
    - **Men who have sex with men**.

- **Injection or noninjection drug use**.
- **Persons experiencing homelessness**.
- **Work with hepatitis A virus** in research laboratory or with nonhuman primates with hepatit
- **Travel in countries with high or intermediate endemic hepatitis A** (HepA-HepB [Twinrix] r to 30 days, followed by a booster dose at 12 months).
- **Close, personal contact with international adoptee** (eg, household or regular babysitting) endemic hepatitis A (administer dose 1 as soon as adoption is planned, at least 2 weeks befo
- **Pregnancy** if at risk for infection or severe outcome from infection during pregnancy.
- **Settings for exposure**, including health care settings targeting services to injection or noninj for developmentally disabled persons (individual risk factor screening not required).

- **Contraindications and precautions:**
  - For contraindications and precautions to hepatitis A (HepA) vaccination, refer to HepA Appendix.

ΔΔ **Hepatitis B vaccination**

- **Routine vaccination:**
  - **Age 19 through 59 years:** Complete a 2- or 3-, or 4-dose series.
    - 2-dose series only applies when 2 doses of Heplisav-B (NOTE: Heplisav-B and PreHevbrio are persons) are used at least 4 weeks apart.
    - 3-dose series Engerix-B, PreHevbrio (NOTE: Heplisav-B and PreHevbrio are not recommended Recombivax HB at 0, 1, 6 months [minimum intervals: dose 1 to dose 2: 4 weeks / dose 2 to d
    - 3-dose series HepA-HepB (Twinrix at 0, 1, 6 months [minimum intervals: dose 1 to dose 2: 4 w
    - 4-dose series HepA-HepB (Twinrix) accelerated schedule of 3 doses at 0, 7, and 21 to 30 days,
  - **Age 60 years or older with** known risk factors for hepatitis B virus infection **should** complete a H
  - **Age 60 years or older without** known risk factors for hepatitis B virus infection **may** complete a
    - **Risk factors for hepatitis B virus infection include:**
      - **Chronic liver disease** (eg, persons with hepatitis C, cirrhosis, fatty liver disease, alcoholic aspartate aminotransferase [AST] level greater than twice upper limit of normal).
      - **HIV infection**.
      - **Sexual exposure risk** (eg, sex partners of hepatitis B surface antigen [HBsAg]-positive pe persons seeking evaluation or treatment for a sexually transmitted infection; men who ha
      - **Current or recent injection drug use**.
      - **Percutaneous or mucosal risk for exposure to blood** (eg, household contacts of HBsAg disabled persons; health care and public safety personnel with reasonably anticipated risl maintenance dialysis, including in-center or home hemodialysis and peritoneal dialysis, a
      - **Incarceration**.
      - **Travel in countries with high or intermediate endemic hepatitis B**.
- **Special situations:**
  - **Patients on dialysis:** complete a 3- or 4-dose series.
    - 3-dose series Recombivax HB at 0, 1, 6 months (NOTE: use Dialysis Formulation 1 mL = 40 mc
    - 4-dose series Engerix-B at 0, 1, 2, and 6 months (NOTE: use 2 mL dose instead of the normal a
- **Contraindications and precautions:**
  - For contraindications and precautions to hepatitis B (HepB) vaccination, refer to HepB Appendix.

◇◇ **Meningococcal vaccination**

- **Special situations for MenACWY:**
  - **Anatomical or functional asplenia (including sickle cell disease), HIV infection, persistent c eculizumab, ravulizumab) use:** 2-dose series MenACWY-D (Menactra, Menveo, or MenQuadfi) a

- **Travel in countries with hyperendemic or epidemic meningococcal disease, or microbiologi** (Menactra, Menveo, or MenQuadfi) and revaccinate every 5 years if risk remains.
- **First-year college students who live in residential housing (if not previously vaccinated at a** Menveo, or MenQuadfi).
- For MenACWY **booster dose recommendations** for groups listed under "Special situations" and among men who have sex with men) and additional meningococcal vaccination information, refe

▪ **Shared clinical decision-making for MenB:**
- **Adolescents and young adults age 16 to 23 years (age 16 to 18 years preferred) not at increa** making, 2-dose series MenB-4C (Bexsero) at least 1 month apart or 2-dose series MenB-FHbp (Tru after dose 1, administer dose 3 at least 4 months after dose 2); MenB-4C and MenB-FHbp are not

▪ **Special situations for MenB:**
- **Anatomical or functional asplenia (including sickle cell disease), persistent complement co ravulizumab) use, or microbiologists routinely exposed to *Neisseria meningitidis*** (NOTE: Men if indicated, but at a different anatomic site, if feasible)**:** 2-dose primary series MenB-4C (Bexsero) at 0, 1 to 2, 6 months (if dose 2 was administered at least 6 months after dose 1, dose 3 not need dose should be administered at least 4 months after dose 3); MenB-4C and MenB-FHbp are not in booster 1 year after primary series and revaccinate every 2 to 3 years if risk remains.
- **Pregnancy:** Delay MenB until after pregnancy unless at increased risk and vaccination benefits o
- For MenB **booster dose recommendations** for groups listed under "Special situations" and in an among men who have sex with men) and additional meningococcal vaccination information, refe

▪ **Contraindications and precautions:**
- For contraindications and precautions to meningococcal ACWY (MenACWY) [MenACWY-CRM (Men MenACWY Appendix.
- For contraindications and precautions to meningococcal B (MenB) [MenB-4C (Bexsero); MenB-FH

§§ ***Haemophilus influenzae*** **type b vaccination**

▪ **Special situations:**
- **Anatomical or functional asplenia (including sickle cell disease):** 1 dose if previously did not r before splenectomy.
- **Hematopoietic stem cell transplant (HSCT):** 3-dose series 4 weeks apart starting 6 to 12 month

▪ **Contraindications and precautions:**
- For contraindications and precautions to *Haemophilus influenzae* type b (Hib) vaccination, refer to

¥¥ Vaccinate after pregnancy.

Reproduced from: Advisory Committee on Immunization Practices. Recommended Adult Immunization Schedule for ages 19 years or https://www.cdc.gov/vaccines/schedules/hcp/imz/adult-conditions.html (Accessed on February 15, 2023).

Graphic 62130 Version 23.0

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Jana Al Hashash, MD, MSc, FACG, AGAF No relevant financial relationship(s) with ineligible companies to disclose. **Miguel Regueiro, MD, AGAF, FACG, FACP** Consultant/Advisory Boards: AbbVie [Crohn disease]; Allergan [Inflammatory bowel disease]; Amgen [Inflammatory bowel disease]; Bristol Myers Squibb [Inflammatory bowel disease]; Celgene [Crohn disease]; Celgene [Inflammatory bowel disease]; Eli Lilly [Inflammatory bowel disease]; Genentech [Inflammatory bowel disease]; Gilead [Inflammatory bowel disease]; Janssen [Crohn disease]; Miraca [Crohn disease]; Pfizer [Inflammatory bowel disease]; Prometheus [Inflammatory bowel disease]; Salix [Inflammatory bowel disease]; Seres [Inflammatory bowel disease]; Takeda [Crohn disease]; TARGET Pharma Solutions [Inflammatory bowel disease]; UCB [Crohn disease]. All of the relevant financial relationships listed have been mitigated. **Sunanda V Kane, MD, MSPH** Grant/Research/Clinical Trial Support: Bristol Myers Squibb [IBD]. Consultant/Advisory Boards: Boehringer Ingelheim [IBD]; Bristol Myers Squibb [IBD]; Fresenius Kabi [IBD]; InveniAI [IBD]; Janssen [IBD]; Lilly [IBD]; Takeda [IBD]; Techlab [IBD]. Other Financial Interest: PredicaMed [Scientific Board]. All of the relevant financial relationships listed have been mitigated. **Kristen M Robson, MD, MBA, FACG** No relevant financial relationship(s) with ineligible companies to disclose.

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Conflict of interest policy

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