Overview of the management of primary biliary cholangitis

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INTRODUCTION

Primary biliary cholangitis (PBC; previously referred to as primary biliary cirrhosis) is characterized by an ongoing immunologic attack on the intralobular bile ducts that leads to chronic cholestasis and cirrhosis. The terminology was changed from primary biliary cirrhosis to primary biliary cholangitis to more accurately describe the disorder and its natural history. The prognosis of patients with PBC has improved greatly because of its diagnosis at earlier stages and the widespread use of ursodeoxycholic acid as treatment.

The goals of management are:

- Suppression of the underlying pathogenic process (ie, destruction of small intralobular hepatic bile ducts)
- Treatment of symptoms that result from chronic cholestasis
- Management of complications that result from chronic cholestasis

The focus of this topic is managing the underlying disease process, symptoms, and complications of PBC. The pathogenesis, clinical manifestations, diagnosis, and prognosis of PBC are discussed separately. (See "Pathogenesis of primary biliary cholangitis (primary biliary cirrhosis)" and "Clinical manifestations, diagnosis, and prognosis of primary biliary cholangitis".)

Indications for and outcomes of liver transplantation for patients with PBC are discussed separately. (See "Liver transplantation in primary biliary cholangitis".)

The overlap syndrome of autoimmune hepatitis with PBC is discussed separately. (See "Autoimmune hepatitis variants: Definitions and treatment".)

Management of patients with cirrhosis is discussed separately. (See "Cirrhosis in adults: Overview of complications, general management, and prognosis".)

MANAGING UNDERLYING DISEASE

General measures — The following measures apply to patients with PBC:

- **Immunizations** – Vaccinations for hepatitis A virus and hepatitis B virus are given to patients without serologic evidence of immunity. Additional vaccines for patients with chronic liver disease include pneumococcal vaccination and immunizations that are given to the general population (eg, influenza) (figure 1 and figure 2). Immunization schedules are described separately. (See "Immunizations for adults with chronic liver disease", section on 'Vaccines in chronic liver disease'.)

- **Abstain from alcohol** – We advise patients to abstain from alcohol and, in particular, to avoid heavy alcohol use (ie, >14 drinks per week or >4 drinks on a given day for men and >7 drinks per week or >3 drinks on a given day for women) [1].

- **Hepatology consultation** – We suggest that patients with PBC are referred to a hepatologist for long-term management.

Pretreatment testing — Prior to initiating pharmacologic therapy, the following laboratory tests are performed (see 'Assessing response' below):

- Serum aminotransferases – Alanine aminotransferase (ALT) and aspartate aminotransferase (AST)
- Alkaline phosphatase
- Total bilirubin
- Gamma-glutamyl transpeptidase
- Platelet count

Baseline laboratory studies are used for assessing disease activity and monitoring response to therapy. (See 'Long-term monitoring' below.)

Therapy to slow disease progression — Approved treatments for PBC include ursodeoxycholic acid (UDCA) and obeticholic acid. However, obeticholic acid is not widely available outside North America. In the absence of obeticholic acid, it is the author's practice to use fibrates in conjunction with UDCA in patients with an inadequate response to UDCA alone. However, evidence to support this approach is limited. (See 'Investigational therapies' below.)

Initial therapy — Initial therapy for all patients with PBC is UDCA at a total daily dose of 13 to 15 mg/kg, given orally and usually administered twice daily (algorithm 1). UDCA is given as long-term therapy because PBC is a chronic disease. Improvement in liver biochemical tests (ie, alkaline phosphatase) is typically observed within three months of starting UDCA, although symptoms such as fatigue often do not improve with treatment. (See 'Managing symptoms' below.)

Liver biochemical testing is performed in three to six months after initiating therapy, while we determine biochemical response (ie, normalization of alkaline phosphatase) after one year of UDCA treatment [2]. (See 'Assessing response' below.)

Approximately 35 percent of patients have an inadequate biochemical response after one year of UDCA, and such patients are evaluated for subsequent treatment options [3,4]. (See 'Subsequent therapy' below and 'Investigational therapies' below.)

For most patients, UDCA is well-tolerated with few adverse effects (eg, modest weight gain [approximately 3 kg]) [5].

For patients with PBC, UDCA as first-line therapy is supported by society guidelines and is associated with a long-term survival benefit, while the risks associated with UDCA are minimal [6,7]. Some meta-analyses and observational studies have demonstrated efficacy of UDCA [8-15]; however, other data have been inconsistent [16,17]. For example, a meta-analysis of 16 randomized trials including 1447 patients found that UDCA had no significant effect on overall or transplant-free mortality [17]. However, the median trial duration in this meta-analysis was two years, which may have been too short to demonstrate a survival benefit. Additionally, various dosing regimens were used, ranging from 7.7 to 15.0 mg/kg per day (median 10 mg/kg per day); thus, dosing in some trials was likely subtherapeutic. Despite these limitations, patients given UDCA had improved liver biochemistries (ie, alkaline phosphatase and total bilirubin) and a lower risk of histologic disease progression (risk ratio [RR] 0.62, 95% 0.44-0.88) compared with placebo [17].

Long-term cohort studies have suggested a survival benefit with UDCA therapy. In a systematic review of studies conducted by the Global PBC Study Group that included 4845 patients, UDCA

was associated with higher rates of transplant-free survival at 5, 10, and 15 years compared with no treatment (90, 78, and 66 percent versus 79, 59, and 32 percent, respectively) [8].

Additional studies have suggested that UDCA was associated with lower rates of disease progression [18-20]. In a study of 162 paired liver biopsies in patients with PBC, UDCA was associated with lower annual rates of progression to advanced fibrosis or cirrhosis compared with placebo (7 versus 34 percent) [18].

For patients with PBC and cirrhosis, response to UDCA therapy has been associated with lower risk of cirrhosis-related complications. In a Veterans Administration database study, 501 patients with PBC and compensated cirrhosis who were treated with UDCA were identified (ie, 287 responders [defined as alkaline phosphatase <1.67 times the upper limit of normal after 24 months of therapy] with 1693 patient-years of follow up and 214 partial responders with 834 patient-years of follow-up) [21]. Response to UDCA was associated with lower risk of hepatic decompensation (adjusted hazard ratio [aHR] 0.54, 95% CI 0.31-0.95), all-cause mortality or transplantation (aHR 0.49, 95% CI 0.33-0.72), and liver-related mortality or transplantation (aHR 0.40, 95% CI 0.24-0.67) compared with partial or no response, after adjusting for patient characteristics such as age, sex, tobacco use, and body mass index. In a trial including 180 patients with PBC who had endoscopic surveillance every two years, UDCA resulted in lower rates of developing esophageal varices compared with placebo after four years' follow-up (16 versus 58 percent) [22].

UDCA, a hydrophilic bile acid, is thought to exert its beneficial effects in cholestatic liver disorders through several mechanisms of action [23,24]:

- Increased hydrophilic index of the circulating bile acid pool
- Stimulation of hepatocellular and ductular secretions
- Cytoprotection against hydrophobic bile acid- and cytokine-induced injury
- Immunomodulation and antiinflammatory effects

Subsequent therapy — For patients with an inadequate response to UDCA (ie, alkaline phosphatase above the upper limit of normal after one year of UDCA) but without cirrhosis, obeticholic acid can be used in combination with UDCA (algorithm 1) [6,25,26]. Obeticholic acid can also be used as monotherapy for patients without cirrhosis who are unable to tolerate UDCA [26]. However, obeticholic acid is contraindicated in patients with decompensated cirrhosis (Child-Pugh class B or C), a prior decompensation event (gastroesophageal varices, encephalopathy), or compensated cirrhosis with portal hypertension because hepatic decompensation and liver failure have been reported with obeticholic acid use in such patients

[6,27-29]. (See "Cirrhosis in adults: Overview of complications, general management, and prognosis", section on 'Child-Pugh classification'.)

Improvement in liver tests typically occurs within six months of therapy with obeticholic acid in combination with UCDA, and biochemical response is defined as alkaline phosphatase ≤1.67 times upper limit of normal [25,26]. (See 'Assessing response' below.)

Evidence from randomized trials suggested that obeticholic acid improved liver biochemical tests in patients with PBC [25,30]. In a 12-month trial including 217 patients with PBC who had inadequate response or intolerance to UDCA, patients were randomly assigned to three groups: obeticholic acid 5 mg daily (with an option to titrate to 10 mg daily), 10 mg daily, or placebo [25]. Patients in the active treatment groups had higher rates of biochemical response (defined as alkaline phosphatase <1.67 times the upper limit of normal and ≤15 percent from baseline value, and a normal bilirubin) compared with placebo (46 and 47 percent, respectively, versus 10 percent) [25]. Pruritus was more common in the obeticholic acid groups compared with placebo (56 and 68 percent, respectively, versus 38 percent).

Long-term cohort studies in patients with PBC suggested a survival benefit with obeticholic acid [31,32]. In a study using propensity score matching, 209 patients treated with obeticholic acid were compared with untreated patients from two disease registries (Global PBC, n = 1381 and UK-PBC, n = 2135) after six years of follow-up [31]. Obeticholic acid was associated with lower risk of mortality or liver transplantation compared with no obeticholic acid use (2 versus 10 and 13 percent, respectively; HR 0.29, 95% CI 0.10-0.83 and HR 0.30, 95% CI 0.12-0.75, respectively). These data lend support for long-term therapy with obeticholic acid.

Obeticholic acid is a derivative of the primary human bile acid chenodeoxycholic acid (CDCA) and is a ligand for the farnesoid X receptor, which plays a role in bile acid homeostasis. Obeticholic acid is a more potent agonist of the receptor (approximately 100-fold higher potency) than CDCA [33,34].

Assessing response — Patients on pharmacologic therapy to slow disease progression (eg, UDCA, obeticholic acid) are monitored with liver biochemical tests (alkaline phosphatase, AST, ALT, and total bilirubin) and platelet count every three to six months to monitor response to therapy and assess disease activity [6]. (See 'Initial therapy' above and 'Subsequent therapy' above.)

Investigational therapies

Fibrates — Fibrates (fenofibrate, a specific peroxisome proliferator-activated receptor [PPAR] alpha agonist, and bezafibrate, a pan-PPAR agonist) have been shown to improve liver

biochemistries in treatment-naïve patients, as well as in patients with incomplete biochemical responses to UDCA [35-40]. In the United States, bezafibrate is not available, while use of other fibrates (eg, fenofibrate) is off-label.

- Bezafibrate – For patients who do not respond to UDCA alone, the author uses bezafibrate in combination with UDCA, as bezafibrate is available in France but is not available in the United States. Patients who respond have alkaline phosphatase ≤1.5 times the upper limit of normal after three to six months of bezafibrate therapy. (See 'Assessing response' above.)

  Bezafibrate was effective for achieving biochemical response in patients with PBC. In a 24-month trial including 100 patients with incomplete biochemical response to UDCA, patients receiving bezafibrate (400 mg daily) plus UDCA were more likely to achieve complete biochemical response compared with patients given placebo plus UDCA (31 versus 0 percent; difference, 31 percentage points, 95% CI 10-50) [39]. Biochemical response was defined as normal levels of alkaline phosphatase, AST, ALT, total bilirubin, and albumin as well as a normal prothrombin index (a derived measure of prothrombin time). Serious adverse events occurred in 14 of 50 patients (28 percent) in the bezafibrate group and in 12 of 50 patients (24 percent) in the placebo group.

  Long-term cohort studies suggested a survival benefit with bezafibrate [41,42]. In a study including nearly 4000 patients with PBC, combination therapy with bezafibrate plus UDCA was associated with lower risk of overall mortality and liver-related mortality compared with UDCA alone (adjusted HR 0.33, 95% CI 0.19-0.55 and 0.27, 95% CI 0.13-0.57, respectively) [42].

- Fenofibrate – In a retrospective study of 120 patients with an incomplete response to UDCA, the addition of fenofibrate was associated with a decreased risk of achieving a composite endpoint of mortality, hepatic decompensation, or liver transplantation (adjusted hazard ratio [HR] 0.40, 95% CI 0.17-0.93) [40].

Adding a fibrate to UDCA therapy has other potential benefits including improvements in symptoms such as itching and fatigue [38,39]. For example, in a study of 48 patients with PBC treated with UDCA, adjuvant therapy with bezafibrate (400 mg daily) resulted in partial or complete relief from itching in 23 of 24 patients (96 percent) in whom itching was assessed [38].

Other drugs — Budesonide is a glucocorticoid with high first-pass metabolism within the liver, resulting in fewer systemic side effects compared with prednisolone. Use of budesonide is reserved for patients without cirrhosis but with marked inflammatory changes on liver biopsy who have not responded to first- and second-line therapies. (See "Overview of budesonide

therapy for adults with inflammatory bowel disease", section on 'Pharmacology' and 'Initial therapy' above and 'Subsequent therapy' above.)

Whether budesonide is beneficial for patients with PBC is uncertain. Two randomized trials showed budesonide combined with UDCA to be more effective in improving liver biochemistries and histology than UDCA alone in patients with PBC [43,44]. However, a small study including nonresponders to UDCA found minimal benefit for adding budesonide to UDCA therapy, while budesonide was associated with decreased bone mineral density [45].

Drugs of uncertain or no benefit — For patients with PBC, we do not use colchicine [46,47] or methotrexate [48] because data have not established drug efficacy. Thus, their role remains uncertain.

Other drugs have been studied for treating PBC, but none of them have been beneficial. These include penicillamine [49,50], cyclosporine [51], prednisolone [52], mycophenolate mofetil [53], and silymarin [54].

Liver transplantation — Liver transplantation is an option for patients with progressive disease despite medical therapy (eg, decompensated cirrhosis with complications such as variceal bleeding and hepatocellular carcinoma). Patient selection for transplantation, timing of transplantation and outcomes in patients with PBC are discussed separately. (See "Liver transplantation in primary biliary cholangitis".)

MANAGING SYMPTOMS

Pruritus — Pruritus is a characteristic cholestatic symptom in patients with PBC, and the approach to management is discussed separately. (See "Pruritus associated with cholestasis".)

Fatigue — Fatigue is common in patients with PBC and can impact quality of life. Fatigue may have several contributing causes (eg, hypothyroidism, sleep disorder), and the evaluation of the patient with fatigue is discussed separately. (See "Approach to the adult patient with fatigue".)

There is no specific therapy for treating fatigue associated with PBC, although various agents have been studied [55-58]. In addition, liver transplantation did not consistently improve some systemic symptoms, particularly fatigue [59]. (See "Liver transplantation in primary biliary cholangitis", section on 'Outcome after liver transplantation'.)

Dry eyes or mouth — The following measures can be used for patients with PBC with dryness of the eyes or mouth (xerostomia) [6]:

- For dry eyes, artificial tears can be used initially, while other agents (eg, cyclosporine ophthalmic emulsion) can be used in those refractory to initial measures, preferably under the supervision of an ophthalmologist. Management of dry eye disease is discussed in more detail separately. (See "Dry eye disease".)

- For dry mouth and dysphagia, saliva substitutes can be tried. For example, pilocarpine can be used in patients who remain symptomatic despite saliva substitutes. (See "Treatment of dry mouth and other non-ocular sicca symptoms in Sjögren's disease", section on 'Treatment of dry mouth'.)

LONG-TERM MONITORING

Our approach to long-term monitoring for patients with PBC includes [6]:

- Liver biochemical and function tests (alanine aminotransferase [ALT], aspartate aminotransferase [AST], alkaline phosphatase, and total bilirubin) and platelet count every three to six months.

- Vitamin A level, vitamin D level, and prothrombin time annually. (See 'Fat-soluble vitamins' below.)

- Thyroid-stimulating hormone annually to screen for hypothyroidism. Hypothyroidism is common in patients with PBC and may coexist at diagnosis or develop during the course of disease [60]. (See "Disorders that cause hypothyroidism", section on 'Chronic autoimmune (Hashimoto's) thyroiditis'.)

  Diagnosis and management of hypothyroidism is discussed separately. (See "Diagnosis of and screening for hypothyroidism in nonpregnant adults" and "Treatment of primary hypothyroidism in adults".)

- Bone mineral densitometry every two years. (See "Evaluation and treatment of low bone mass in primary biliary cholangitis (primary biliary cirrhosis)".)

- For patients with cirrhosis:

  - Upper endoscopy every two to three years to screen for gastroesophageal varices.

  - Liver ultrasound every six months to screen for hepatocellular carcinoma. (See "Surveillance for hepatocellular carcinoma in adults".)

COMPLICATIONS

Cholestasis-related issues

Metabolic bone disease — The evaluation and treatment of low bone mass in patients with PBC is discussed separately. (See "Evaluation and treatment of low bone mass in primary biliary cholangitis (primary biliary cirrhosis)".)

Fat malabsorption — For patients with PBC who are jaundiced, chronic cholestasis and subsequent reduced bile acid secretion may result in fat malabsorption [61,62]. (See "Overview of nutrient absorption and etiopathogenesis of malabsorption".)

Management of fat malabsorption includes restriction of dietary fat and supplementation with medium-chain triglycerides (MCTs) if caloric supplementation is required to maintain body weight. The digestion and absorption of MCTs are not nearly as dependent upon bile acids as are the long-chain fatty acids, which are the major constituent of dietary triglycerides. Treatment of malabsorption is discussed in more detail separately. (See "Overview of the treatment of malabsorption in adults", section on 'General management'.)

Clinical manifestations of fat malabsorption include diarrhea and weight loss, and these are discussed separately [63]. (See "Approach to the adult patient with suspected malabsorption".)

Fat-soluble vitamins — Patients with PBC (especially those with jaundice and/or on the transplantation waiting list) are at risk for deficiencies in the fat-soluble vitamins A, D, E, and K [64]. (See 'Long-term monitoring' above.).

For patients with fat-soluble vitamin deficiency, supplementation with water-soluble preparations is discussed separately. (See "Overview of the treatment of malabsorption in adults", section on 'Nutrient repletion and supplementation'.)

Hypercholesterolemia — Hypercholesterolemia (ie, cholesterol values above 200 mg/dL [5.2 mmol/L]) is a common feature of PBC, and the clinical features and management of hypercholesterolemia are discussed separately. (See "Hypercholesterolemia in primary biliary cholangitis (primary biliary cirrhosis)".)

Xanthomas — Cutaneous xanthomas (ie, deposits of cholesterol in the skin) associated with hyperlipidemia are usually asymptomatic, although treatment may be desired for cosmetic reasons (picture 1). (See "Clinical manifestations, diagnosis, and prognosis of primary biliary cholangitis", section on 'Clinical manifestations'.)

Pharmacologic treatment of dyslipidemia often leads to improvement in xanthomas caused by hyperlipidemia. The xanthoma types and treatment of cutaneous xanthomas are discussed separately. (See "Cutaneous xanthomas".)

Cirrhosis-related issues

Portal hypertension — Patients with PBC may develop portal hypertension as a result of biliary cholangitis, and complications of portal hypertension (eg, variceal bleeding, ascites) are discussed separately. (See "Cirrhosis in adults: Overview of complications, general management, and prognosis" and "Portal hypertension in adults".)

Patients with PBC who have developed complications of cirrhosis and portal hypertension (eg, ascites, spontaneous bacterial peritonitis, variceal bleeding), are regarded as having decompensated cirrhosis and have a worse prognosis than those with cirrhosis but without complications. (See "Clinical manifestations, diagnosis, and prognosis of primary biliary cholangitis", section on 'Prognosis'.)

Hepatocellular carcinoma — Patients with PBC and cirrhosis are at risk for developing hepatocellular carcinoma, and this is discussed separately. (See "Clinical manifestations, diagnosis, and prognosis of primary biliary cholangitis", section on 'Hepatocellular carcinoma'.)

The approach to surveillance for HCC in high-risk patients is discussed separately. (See "Surveillance for hepatocellular carcinoma in adults".)

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: Primary biliary cholangitis".)

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 topic (see "Patient education: Primary biliary cholangitis (primary biliary cirrhosis) (The Basics)")

SUMMARY AND RECOMMENDATIONS

- **Background** – Primary biliary cholangitis (PBC; previously referred to as primary biliary cirrhosis) is characterized by an ongoing immunologic attack on the intralobular bile ducts that leads to chronic cholestasis and cirrhosis. The goals of management are (see 'Introduction' above):
  - Suppression of the underlying pathogenic process (ie, destruction of small intralobular hepatic bile ducts)
  - Treatment of symptoms that result from chronic cholestasis
  - Management of complications that result from chronic cholestasis
- **General measures** – The following measures apply to all patients with PBC (see 'General measures' above):
  - Immunizations – Vaccinations for hepatitis A virus and hepatitis B virus are given to patients without serologic evidence of immunity. Additional vaccines for patients with chronic liver disease include pneumococcal vaccination and immunizations that are given to the general population (eg, influenza). Immunization schedules are described separately. (See "Immunizations for adults with chronic liver disease", section on 'Vaccines in chronic liver disease'.)
  - Abstain from alcohol – We advise patients to refrain from alcohol and, in particular, to avoid heavy alcohol use (ie, >14 drinks per week or >4 drinks on a given day for men and >7 drinks per week or >3 drinks on a given day for women).
  - Hepatology consultation for long-term management.
- **Pharmacologic therapy** – Pharmacologic therapy for PBC includes (algorithm 1):

- For all patients with PBC, we suggest ursodeoxycholic acid (UDCA) as first-line therapy because it improved liver biochemical tests and was associated with slower disease progression and improved long-term survival (**Grade 2C**). Hepatology experts routinely use UDCA 13 to 15 mg/kg per day, typically given in two divided doses and continued indefinitely because of the chronic nature of PBC. (See 'Initial therapy' above.)

- For patients with an inadequate response or intolerance to UDCA but who do not have cirrhosis, we suggest subsequent therapy with obeticholic acid (where available), used in combination with UDCA or as monotherapy (**Grade 2C**). Obeticholic acid improved liver biochemical tests in randomized trials and was associated with a survival benefit in cohort studies with long-term follow-up. (See 'Subsequent therapy' above.)

- For patients with an inadequate response to UDCA and without access to obeticholic acid, the author uses bezafibrate in combination with UDCA because it improved liver biochemistries and was associated with a survival benefit. (See 'Investigational therapies' above.)

- **Liver transplantation** – Patient selection for transplantation, timing of transplantation, and outcomes in patients with PBC are discussed separately. (See "Liver transplantation in primary biliary cholangitis".)

- **Managing symptoms** – Pruritus is a characteristic cholestatic symptom in patients with PBC, and management of pruritus is discussed separately. (See "Pruritus associated with cholestasis".)

- **Long-term monitoring** – Our approach to long-term monitoring for patients with PBC includes (see 'Long-term monitoring' above):

  - Liver biochemical and function tests (alanine aminotransferase [ALT], aspartate aminotransferase [AST], alkaline phosphatase and total bilirubin) and platelet count every three to six months

  - Vitamin A, vitamin D, and prothrombin time annually

  - Thyroid-stimulating hormone annually

  - Bone mineral densitometry every two years

  - For patients with PBC and cirrhosis:

    - Upper endoscopy every two to three years to screen for gastroesophageal varices

- Liver ultrasound every six months to screen for HCC

The evaluation and treatment of low bone mass in patients with PBC is discussed separately. (See "Evaluation and treatment of low bone mass in primary biliary cholangitis (primary biliary cirrhosis)".)

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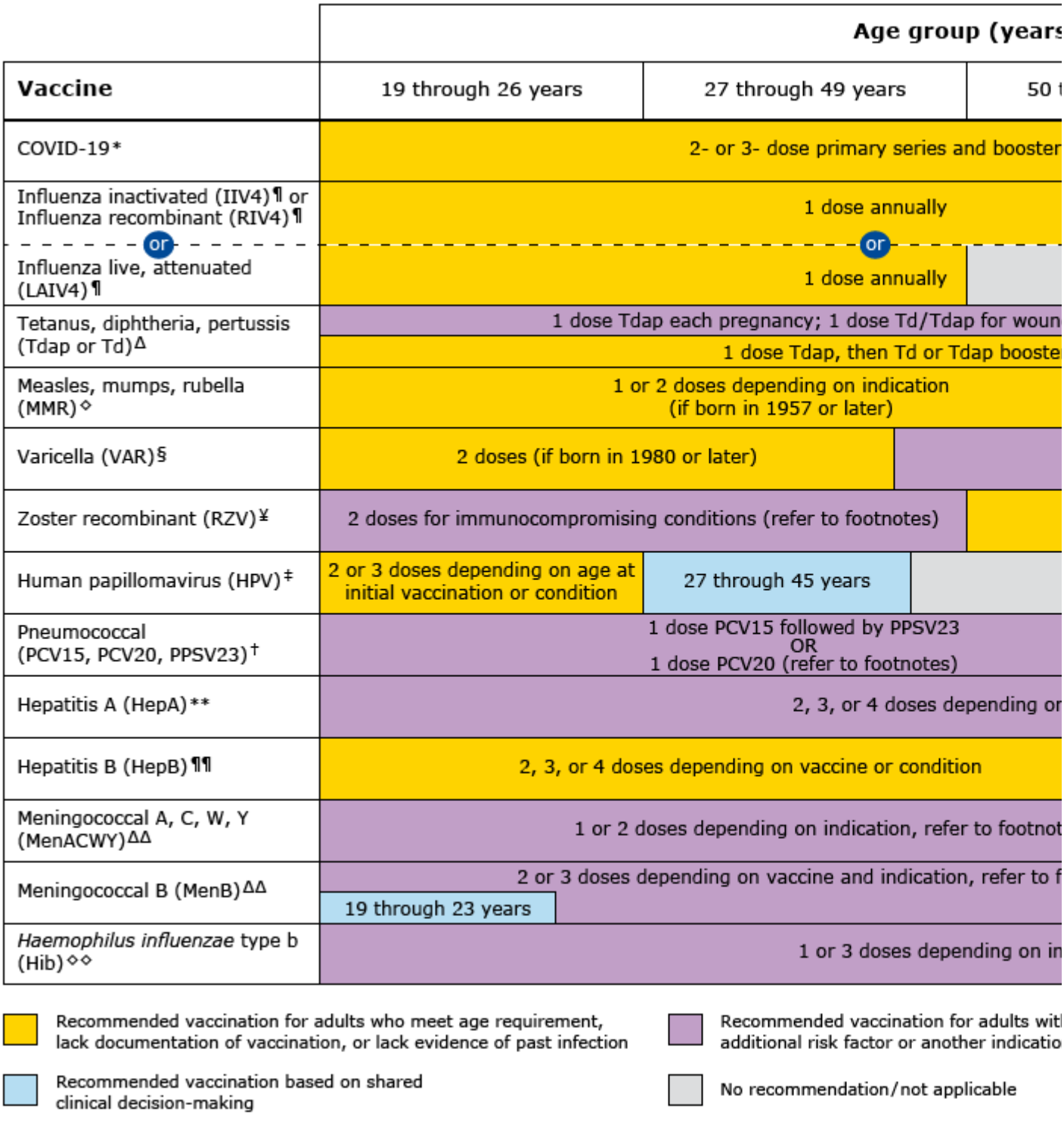
Topic 3623 Version 48.0

GRAPHICS

Recommended adult immunization schedule by age group - United States, 2023



Administer recommended vaccines if vaccination history is incomplete or unknown. Do not restart or add d between doses. The use of trade names is for identification purposes only and does not imply endorsement

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 series.
    - **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.

*** 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 www.cdc.gov/vaccines/covid-19/clinical-considerations/interim-considerations-us.html#immur
  - **For Janssen COVID-19 Vaccine recipients** refer to COVID-19 schedule at www.cdc.gov/vaccines/c considerations-us.html.
  - **NOTE:** Current COVID-19 schedule available at www.cdc.gov/vaccines/covid-19/downloads/COVID- For more information on Emergency Use Authorization (EUA) indications for COVID-19 vaccines, p and-response/coronavirus-disease-2019-covid-19/covid-19-vaccines.
- **Contraindications and precautions:**
  - Refer to contraindications and precautions to COVID-19 vaccination.

¶ 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), or quadrivalent adjuvanted inactivated influenza vaccine (aIIV4) is preferred. If none of these thre appropriate influenza vaccine should be used.
  - 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 intervention): Any influenza vaccine appropriate for age and health status may be administered. If medical setting under supervision of health care provider who can recognize and manage severe
  - **Close contacts (eg, caregivers, health care workers) of severely immunosuppressed persons** persons should not receive LAIV4. If LAIV4 is given, they should avoid contact with/caring for such vaccination.

- **Severe allergic reaction (eg, anaphylaxis) to a vaccine component or a previous dose of any i** contraindications and precautions.
- **History of Guillain-Barré syndrome within 6 weeks after previous dose of influenza vaccine:** vaccination benefits outweigh risks for those at higher risk for severe complications from influenz

▪ **Contraindications and precautions:**

- For contraindications and precautions to influenza vaccination, refer to IIV4 Appendix, LAIV4 Appe

Δ **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 weeks later and a third dose of Td or Tdap 6 to 12 months later (Tdap can be substituted for any T 10 years thereafter.
- **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 more than 10 years since last dose of tetanus-toxoid-containing vaccine; for all other wounds, adr dose of tetanus-toxoid-containing vaccine. Tdap is preferred for persons who have not previously tetanus-toxoid-containing vaccine is indicated for a pregnant woman, use Tdap. For detailed infor 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 immunity or disease (diagnosis of disease without laboratory confirmation is not evidence of i

▪ **Special situations:**

- **Pregnancy with no evidence of immunity to rubella:** MMR contraindicated during pregnancy; a facility), 1 dose.
- **Nonpregnant persons 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 mumps, or rubella:** 2-dose series at least 4 weeks apart; MMR contraindicated for HIV infection w cells/mm^3.
- **Severe immunocompromising conditions:** MMR contraindicated.
- **Students in postsecondary educational institutions, international travelers, and household immunocompromised persons with no evidence of immunity to measles, mumps, or rubella** did not receive any doses of MMR or 1 dose if previously received 1 dose MMR.
- **In mumps outbreak settings**, for information about additional doses of MMR (including 3rd dos https://www.cdc.gov/mmwr/volumes/67/wr/mm6701a7.htm.
- **Health care personnel:**
  - **Born before 1957 with no evidence of immunity to measles, mumps, or rubella:** Consider against measles or mumps or 1 dose for protection against rubella.
  - **Born in 1957 or later with no evidence of immunity to measles, mumps, or rubella:** 2-dos measles or mumps or at least 1 dose for protection against 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 [measles-mumps-rubella-varicella vaccine] for children); if previously received 1 dose varicella-con dose.
    - **Evidence of immunity:** US-born before 1980 (except for pregnant women and health care per varicella-containing vaccine at least 4 weeks apart, diagnosis or verification of history of varice laboratory evidence of immunity or disease.
- **Special situations:**
  - **Pregnancy with no evidence of immunity to varicella:** VAR contraindicated during pregnancy; a facility), 1 dose if previously received 1 dose varicella-containing vaccine or dose 1 of 2-dose series receive any varicella-containing vaccine, regardless of whether US-born before 1980.
  - **Health care personnel with no evidence of immunity to varicella:** 1 dose if previously received to 8 weeks apart if previously did not receive any varicella-containing vaccine, regardless of wheth
  - **HIV infection with CD4 percentages ≥15% and CD4 count ≥200 cells/mm^3 with no evidence** doses 3 months apart); VAR contraindicated for HIV infection with CD4 percentage <15% or CD4 c
  - **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 susceptibility becomes available, providers should follow ACIP guidelines for varicella vaccination varicella, and there are limited data on the use of RZV in persons without a history of varicella or v zoster vaccine (RZV, Shingrix) 2 to 6 months apart (minimum interval: 4 weeks; repeat dose if adm zoster or history of zoster vaccine live (ZVL, Zostavax) vaccination.
- **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 varicella vaccination, or herpes zoster, providers should refer to the clinical considerations for use years and the ACIP varicella vaccine recommendations for further guidance: www.cdc.gov/mmwr/ recombinant zoster vaccine (RZV, Shingrix) 2 to 6 months apart (minimum interval: 4 weeks; repea information, refer to www.cdc.gov/shingles/vaccination/immunocompromised-adults.html.
- **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 to dose 3: 12 weeks / 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 needed.
  - **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 t**
- **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 dec**
    - **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 needed if inadvertently 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 vaccination** PCV20. If PCV15 is used, this should be followed by a dose of PPSV23 given at least 1 year after between PCV15 and PPSV23 can be considered for adults with an immunocompromising cond include chronic renal failure, nephrotic syndrome, immunodeficiency, iatrogenic immunosupp immunodeficiency virus, Hodgkin disease, leukemia, lymphoma, multiple myeloma, solid orga cell disease, or other hemoglobinopathies), cochlear implant, or cerebrospinal fluid leak to mi caused by serotypes unique to PPSV23 in these vulnerable groups.
    - **Previously received only PCV7:** Follow the recommendation above.
    - **Previously received only PCV13:** 1 dose PCV20 at least 1 year after the PCV13 dose OR compl here: https://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 PPS by another dose of PPSV23.
    - **Previously received both PCV13 and PPSV23 but NO PPSV23 was received at age 65 years** last pneumococcal vaccine dose OR complete the recommended PPSV23 series as described h www.cdc.gov/vaccines/vpd/pneumo/downloads/pneumo-vaccine-timing.pdf.
    - **Previously received both PCV13 and PPSV23, AND PPSV23 was received at age 65 years or** dose of PCV20 at least 5 years after the last pneumococcal vaccine dose.
    - For guidance on determining which pneumococcal vaccines a patient needs and when, please here: 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** factors include alcoholism, chronic heart/liver/lung disease, chronic renal failure, cigarette smokir CSF leak, diabetes mellitus, generalized malignancy, HIV, Hodgkin disease, immunodeficiency, iatr multiple myeloma, nephrotic syndrome, solid organ transplants, or sickle cell disease, or other he
    - **Not previously received a PCV13, PCV15, or PCV20 or whose previous vaccination history** PCV15 is used, this should be followed by a dose of PPSV23 given at least 1 year after the PCV1 PCV15 and PPSV23 can be considered for adults with an immunocompromising condition (NO chronic renal failure, nephrotic syndrome, immunodeficiency, iatrogenic immunosuppression, virus, Hodgkin disease, leukemia, lymphoma, multiple myeloma, solid organ transplants, conc other hemoglobinopathies), cochlear implant, or cerebrospinal fluid leak.
    - **Previously received only PCV7:** Follow the recommendation above.
    - **Previously received only PCV13:** 1 dose PCV20 at least 1 year after the PCV13 dose OR compl here: 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 PPS by another dose of PPSV23.
- **Previously received both PCV13 and PPSV23 but have not completed the recommended s** pneumococcal vaccine dose OR complete the recommended PPSV23 series as described here: www.cdc.gov/vaccines/vpd/pneumo/downloads/pneumo-vaccine-timing.pdf.

- For guidance on determining which pneumococcal vaccines a patient needs and when, please refe www.cdc.gov/vaccines/vpd/pneumo/hcp/pneumoapp.html.

- **Contraindications and precautions:**
  - For contraindications and precautions to Pneumococcal conjugate (PCV15 and PCV20), refer to PC (PPSV23), refer to PPSV23 Appendix.

** **Hepatitis A vaccination**

- **Routine vaccination:**
  - **Not at risk but want protection from hepatitis A (identification of risk factor not required):** Vaqta 6 to 18 months apart [minimum interval: 6 months]) or 3-dose series HepA-HepB (Twinrix a 2: 4 weeks / dose 2 to dose 3: 5 months]).
- **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 aminotransferase [ALT] or aspartate aminotransferase [AST] level greater than twice the upp
    - **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 doses at 0, 7, and 21 to 30 days, followed by a booster dose at 12 months).
    - **Close, personal contact with international adoptee** (eg, household or regular babysitting) or intermediate endemic hepatitis A (administer dose 1 as soon as adoption is planned, at lea
    - **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 nonresidential day care facilities for developmentally disabled persons (individual risk factor s
- **Contraindications and precautions:**
  - For contraindications and precautions to hepatitis A (HepA) vaccination, refer to HepA Appendix.

¶¶ **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 data in pregnant persons) are used at least 4 weeks apart.
    - 3-dose series Engerix-B, PreHevbrio (NOTE: Heplisav-B and PreHevbrio are not recommended persons), or Recombivax HB at 0, 1, 6 months [minimum intervals: dose 1 to dose 2: 4 weeks weeks]).
    - 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 infection include:**
  - **Chronic liver disease** (eg, persons with hepatitis C, cirrhosis, fatty liver disease, alcoholic aminotransferase [ALT] or aspartate aminotransferase [AST] level greater than twice uppe
  - **HIV infection**.
  - **Sexual exposure risk** (eg, sex partners of hepatitis B surface antigen [HBsAg]-positive pe monogamous relationships; persons seeking evaluation or treatment for a sexually transı
  - **Current or recent injection drug use**.
  - **Percutaneous or mucosal risk for exposure to blood** (eg, household contacts of HBsAg developmentally disabled persons; health care and public safety personnel with reasonab contaminated body fluids; persons on maintenance dialysis, including in-center or home who are predialysis; patients with diabetes).
  - **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.

ΔΔ **Meningococcal vaccination**

- **Special situations for MenACWY:**
  - **Anatomical or functional asplenia (including sickle cell disease), HIV infection, persistent c inhibitor (eg, eculizumab, ravulizumab) use:** 2-dose series MenACWY-D (Menactra, Menveo, or every 5 years if risk remains.
  - **Travel in countries with hyperendemic or epidemic meningococcal disease or microbiologis** dose MenACWY (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** MenACWY (Menactra, Menveo, or MenQuadfi).
  - For MenACWY **booster dose recommendations** for groups listed under "Special situations" and organizational settings and among men who have sex with men) and additional meningococcal v www.cdc.gov/mmwr/volumes/69/rr/rr6909a1.htm.
- **Shared clinical decision-making for MenB:**
  - **Adolescents and young adults age 16 to 23 years (age 16 to 18 years preferred) not at increa** shared clinical decision-making, 2-dose series MenB-4C (Bexsero) at least 1 month apart or 2-dos dose 2 was administered less than 6 months after dose 1, administer dose 3 at least 4 months af interchangeable (use same product for all doses in series).
- **Special situations for MenB:**
  - **Anatomical or functional asplenia (including sickle cell disease), persistent complement co eculizumab, ravulizumab) use, or microbiologists routinely exposed to *Neisseria meningitidi*** simultaneously with MenACWY vaccines if indicated but at a different anatomic site, if feasible)**:** 2 month apart or 3-dose primary series MenB-FHbp (Trumenba) at 0, 1 to 2, 6 months (if dose 2 wa 3 not needed; if dose 3 is administered earlier than 4 months after dose 2, a fourth dose should b MenB-4C and MenB-FHbp are not interchangeable (use same product for all doses in series); 1 d 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 ar organizational settings and among men who have sex with men) and additional meningococcal v www.cdc.gov/mmwr/volumes/69/rr/rr6909a1.htm.

- **Contraindications and precautions:**
  - For contraindications and precautions to meningococcal ACWY (MenACWY) [MenACWY-CRM (Mer (MenQuadfi)], refer to 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 preferably at least 14 days before splenectomy.
  - **Hematopoietic stem cell transplant (HSCT):** 3-dose series 4 weeks apart starting 6 to 12 month vaccination history.
- **Contraindications and precautions:**
  - For contraindications and precautions to *Haemophilus influenzae* type b (Hib) vaccination, refer to

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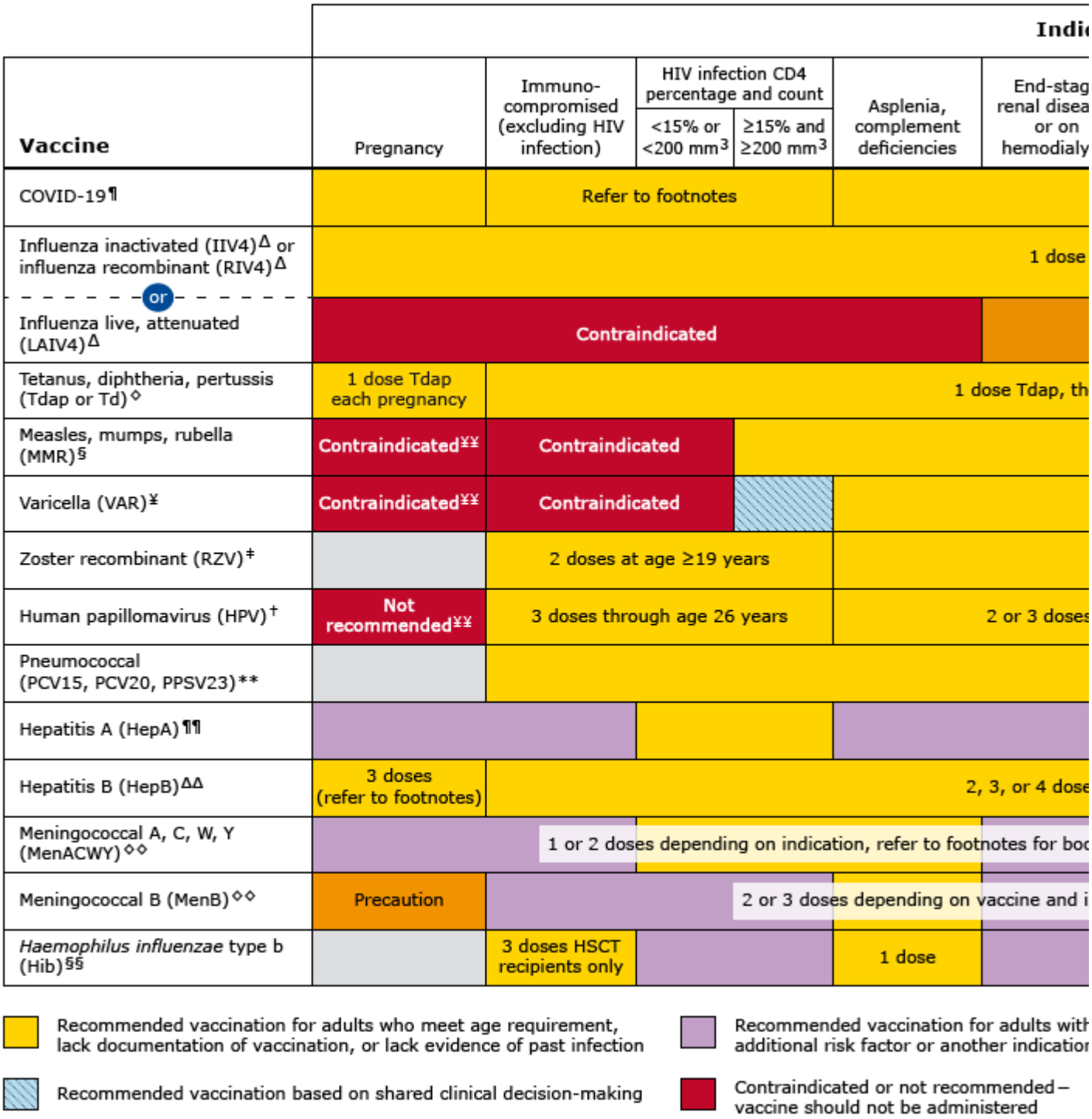
Reproduced from: Advisory Committee on Immunization Practices. Recommended Adult Immunization Schedule for ages 19 years or Prevention. Available at: https://www.cdc.gov/vaccines/schedules/hcp/imz/adult.html (Accessed on February 15, 2023).

Graphic 82634 Version 35.0

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 d 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

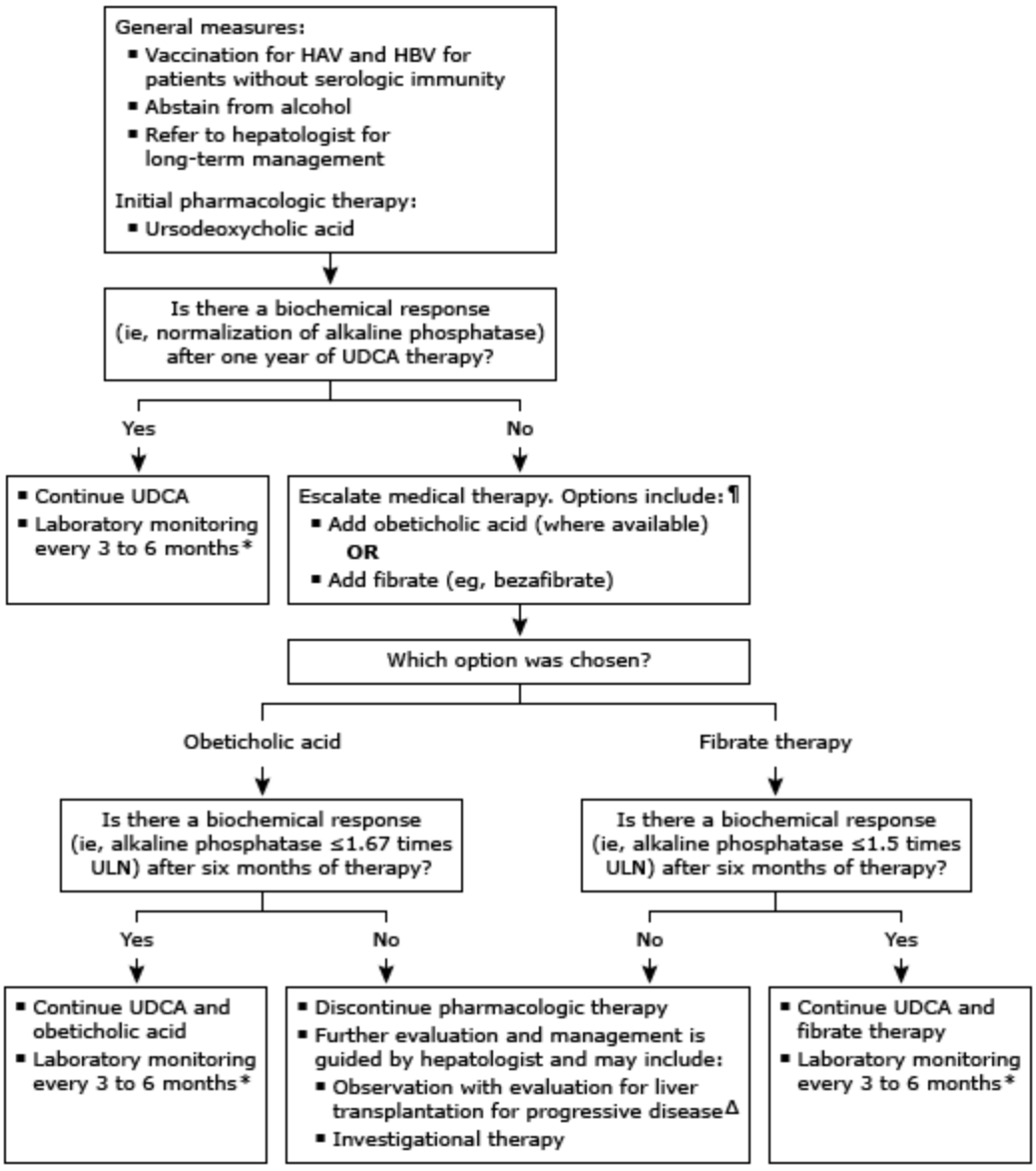
▪ **Contraindications and precautions:**
- For contraindications and precautions to *Haemophilus influenzae* type b (Hib) vaccination, refer to

¥¥ 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

Approach to slowing disease progression for patients with primary biliary cholangitis



Refer to UpToDate content on the management of primary biliary cholangitis.

HAV: hepatitis A virus; HBV: hepatitis B virus; UDCA: ursodeoxycholic acid; OCA: obeticholic acid; ULN: upper limit of normal; ALT: alanine aminotransferase; AST: aspartate aminotransferase.

* Liver biochemical tests (ALT, AST, alkaline phosphatase, and total bilirubin) and platelet count are obtained every 3 to 6 months to assess disease activity and monitor response to therapy.

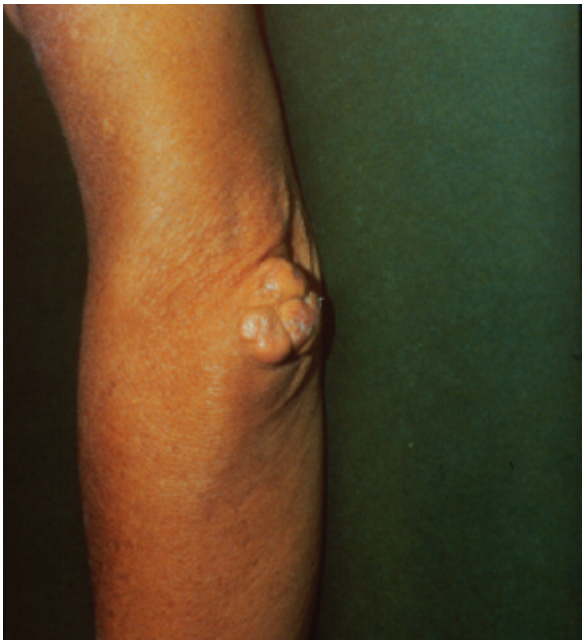
¶ The efficacy of obeticholic acid and bezafibrate appear comparable in this setting, and therapy selection is based on drug availability, clinician preference, and disease severity. Obeticholic acid is not widely available outside of North America, and it is contraindicated in patients with decompensated cirrhosis

(Child-Pugh class B or C; refer to UpToDate calculator for Child-Pugh score for severity of liver disease), a prior decompensation event (gastroesophageal varices, encephalopathy), or compensated cirrhosis with portal hypertension. Bezafibrate is not available in the United States, while use of other fibrates (eg, fenofibrate) is off-label.

Δ Refer to UpToDate content on liver transplantation for patients with primary biliary cholangitis.

Graphic 128215 Version 3.0

Tuberous xanthomas



Tuberous xanthomas on the elbow of a woman with primary biliary cholangitis and a marked elevation in the serum cholesterol concentration (1400 mg/dL [36.4 mmol/L]).

Courtesy of Marshall M Kaplan, MD.

Graphic 75143 Version 2.0

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Raoul Poupon, MD No relevant financial relationship(s) with ineligible companies to disclose. **Keith D Lindor, MD** Consultant/Advisory Boards: Pliant [DSMB member]. 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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