Travel Medicine Made Plane & Simple

28 Years Featuring
South Florida Pharmacy Residents

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Disclosures

- The author of this presentation has nothing to disclose concerning possible financial or personal relationships with commercial entities that may have direct or indirect interests in the subject matter of this presentation

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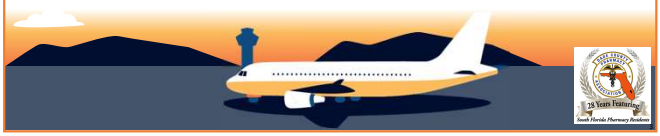
Objectives

1. Describe vaccines available to travelers at risk of exposure to various pathogens
2. Discuss travelers' diarrhea prevention and treatment
3. Discuss malaria prevention
4. Understand travel health concerns and new developments in travel medicine



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Abbreviations

- AKI: Acute kidney injury
- CDC: Centers for Disease Control and Prevention
- CI: Contraindication
- CrCl: Creatinine clearance
- GI: Gastrointestinal
- G6PD: Glucose-6-phosphate dehydrogenase
- HCC: Hepatocellular carcinoma
- IM: Intramuscular
- IPV: Inactivated polio vaccine
- OTC: Over-the-counter
- PO: Per os (by mouth)
- RSV: Respiratory syncytial virus
- Rx: Prescription
- SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2
- STEP: Smart Traveler Enrollment Program
- SubQ: Subcutaneous
- TD: Travelers' diarrhea
- U.S.: United States

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Background

- Travel medicine: Field of medicine focusing on the prevention of disease or other adverse health outcomes in the international traveler
  - Focuses on pretravel preventative care
- 49.1 million outbound departures from the U.S. in 2021
- Increased globalization leads to increased risk of diseases from travel
- Disease transmission through:
  - Food and water
  - Blood and bodily fluids
  - Insects

•David H. National Travel and tourism office fact sheet international visitation. International Trade Administration. 2021. Accessed January 2, 2024. https://www.trade.gov/sites/default/files/2021-01/Fact%20Sheet%20International%20Visitation%20FINAL.pdf
•Hui CP; Canadian Paediatric Society, Infectious Diseases and Immunization Committee. The Committee to Advise on Tropical Medicine and Travel (CATMAT) - a reference for Canadian paediatricians. *Paediatr Child Health*. 2015;20(8):437-440. doi:10.1093/pch/20.8.437

5

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Infections

- Common travel medicine disease states
- Important to prevent and treat in order to improve quality of life short-term and life-long

Meningitis	Japanese Encephalitis
Polio	Yellow Fever
Typhoid Fever	Dengue
Cholera	Travelers' Diarrhea
Hepatitis A	Malaria
Hepatitis B	

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Vaccines for Travelers
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Vaccines for Oral or Fecal-Oral Route Pathogens
18 Years Fostering
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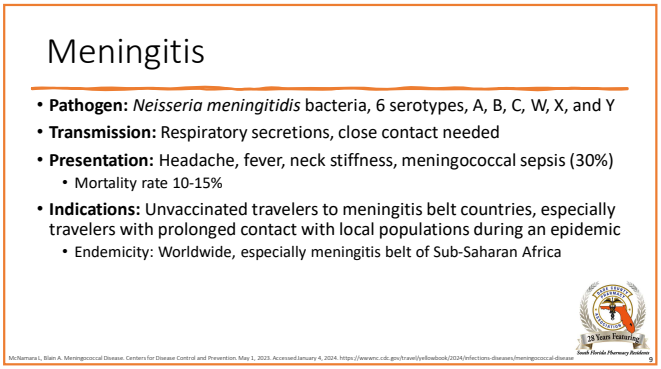
Meningitis
• Pathogen: Neisseria meningitidis bacteria, 6 serotypes, A, B, C, W, X, and Y
• Transmission: Respiratory secretions, close contact needed
• Presentation: Headache, fever, neck stiffness, meningococcal sepsis (30%)
• Mortality rate 10-15%
• Indications: Unvaccinated travelers to meningitis belt countries, especially travelers with prolonged contact with local populations during an epidemic
• Endemicity: Worldwide, especially meningitis belt of Sub-Saharan Africa
18 Years Fostering
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Meningitis Dosing

- **Dosing:**

Routine vaccination	2-dose series given IM at 11-12 years and booster at 16 years
2 months old	4-dose series at 2, 4, 6, and 12 months of age
3-6 months old	3- or 4-dose series at months 0, 2, and 5
7-23 months old	2-dose series at months 0 and 3
≥ 2 years old	1 dose of MenACWY (Menveo® or MenQuadfi®)

  - MenACWY-CRM (Menveo®): Approved for age 2 months to 55 years
  - MenACWY-TT (MenQuadfi®): Approved for age ≥ 2 years

McNamara L, Blain A. Meningococcal Disease. Centers for Disease Control and Prevention. May 1, 2023. Accessed January 4, 2024. https://wwwnc.cdc.gov/travel/yellowbook/2024/infections-diseases/meningococcal-disease

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Polio

- **Pathogen:** Poliovirus, genus *Enterovirus*
- **Transmission:** Person to person through oral and fecal-oral routes
- **Presentation:** Most infections asymptomatic or flu-like symptoms, but 1/200 to 1/2000 associated with paralysis
- **Indications:** Any unvaccinated or under-vaccinated traveler to countries with current or recent poliovirus circulation
  - Endemicity: Type 1 wild poliovirus (WPV) is endemic to Afghanistan and Pakistan only. Circulating vaccine-derived poliovirus (cVDPV) is found in countries in Africa and Asia

Estivariz C, Routh J, Wassilak S. Poliomyelitis. Centers for Disease Control and Prevention. November 28, 2023. Accessed January 4, 2024. https://wwwnc.cdc.gov/travel/yellowbook/2024/infections-diseases/poliomyelitis

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Polio Dosing

- **Dosing:**
  - Routine vaccination: 4-dose series given IM or SubQ at age 2 months, 4 months, 6-18 months, and 4-6 years
  - Unvaccinated adults: 2 doses of Poliovirus Vaccine Inactivated, IPV (IPOL®) given IM or SubQ 4-8 weeks apart, and third dose 6-12 months after second dose
  - One lifetime IPV booster if at increased risk of exposure

Estivariz C, Routh J, Wassilak S. Poliomyelitis. Centers for Disease Control and Prevention. November 28, 2023. Accessed January 4, 2024. https://wwwnc.cdc.gov/travel/yellowbook/2024/infections-diseases/poliomyelitis

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Typhoid Fever

Live Vaccine!

- **Pathogen:** *Salmonella enterica* bacteria, Typhi serotypes
- **Transmission:** Food and water contaminated with fecal matter, contact with acutely infected person or chronic, asymptomatic carrier
- **Presentation:** Fatigue, fever up to 104°F/40°C, anorexia, headache, diarrhea, vomiting
  - Mortality 10-30% when untreated
- **Indications:** Travelers to low and middle-income countries where typhoid and paratyphoid fever are endemic, and travelers to mass gatherings or visiting friends and relatives
  - Endemicity: Africa, Latin America, Asia (especially South Asia)

Hughes M, Appiah G, Watkins L. Typhoid & Paratyphoid Fever. Centers for Disease Control and Prevention. May 1, 2023. Accessed January 4, 2024. https://wwwnc.cdc.gov/travel/yellowbook/2024/infections-diseases/typhoid-and-paratyphoid-fever

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Typhoid Fever Dosing

Live Vaccine!

- **Typhoid Vaccine Live Oral Ty21a (Vivotif®)**: One enteric-coated capsule by mouth 1 hour before a meal with a cold or lukewarm drink every other day for four doses
  - Complete course ≥ 1 week before potential exposure
  - ≥ 6 years old
  - Contraindications to Vivotif®: Pregnant, immunocompromised
- **Typhoid Vi Polysaccharide Vaccine (Typhim Vi®)**: One dose given IM
  - ≥ 2 years old

Hughes M, Appiah G, Watkins L. Typhoid & Paratyphoid Fever. Centers for Disease Control and Prevention. May 1, 2023. Accessed January 4, 2024. https://wwwnc.cdc.gov/travel/yellowbook/2024/infections-diseases/typhoid-and-paratyphoid-fever

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Cholera

Live Vaccine!

- **Pathogen:** *Vibrio cholerae* bacteria
- **Transmission:** Acquired from untreated drinking water most often, also raw or undercooked food, especially seafood
- **Presentation:** Acute watery diarrhea, afebrile. Severe cholera (10%) = profuse watery diarrhea, nausea, vomiting
  - Mortality > 50% if untreated
- **Indications:** Humanitarian aid workers, refugees and internally displaced people, and travelers going to endemic or outbreak areas
  - Endemicity: Africa, Americas, South and Southeast Asia
- **Contraindications:** Pregnant, immunocompromised

Pindyck T, Gutelius B, Mintz E. Cholera. Centers for Disease Control and Prevention. May 1, 2023. Accessed January 4, 2024. https://wwwnc.cdc.gov/travel/yellowbook/2024/infections-diseases/cholera

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Cholera Dosing

Live Vaccine!

- Cholera Vaccine, Live, Oral (Vaxchora®): One oral dose ≥ 10 days before potential exposure
- Dissolve buffer packet in 100 mL of cold or room temperature bottled water, stir in active packet for 30 seconds, and drink within 15 minutes
- Age 2-64 years

vaxchora.com. 2022.

Pindyck T, Gutelius B, Mintz E. Cholera. Centers for Disease Control and Prevention. May 1, 2023. Accessed January 4, 2024. https://wwwnc.cdc.gov/travel/yellowbook/2024/infections-diseases/cholera

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Cholera Dosing

Live Vaccine!

- Age 2-5: Discard half of buffer solution before adding active packet
- May add up to 4 g of sucrose or up to 1 g of non-flavored stevia sweeteners
- No other medicinal flavors → reduced efficacy

Pindyck T, Gutelius B, Mintz E. Cholera. Centers for Disease Control and Prevention. May 1, 2023. Accessed January 4, 2024. https://wwwnc.cdc.gov/travel/yellowbook/2024/infections-diseases/cholera

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Hepatitis A

- **Pathogen:** Hepatitis A virus
- **Transmission:** Fecal-oral route, contaminated food or water
- **Presentation:** Abrupt onset of fever, malaise, anorexia, nausea, abdominal pain, jaundice
  - Mortality 0.3%-1.8%
- **Indications:** Unvaccinated or traveling to areas with inadequate sanitation and limited access to clean water
  - High endemicity: Parts of Africa and Asia

Nelson N, Wieng M. Hepatitis A. Centers for Disease Control and Prevention. May 1, 2023. Accessed January 4, 2024. https://wwwnc.cdc.gov/travel/yellowbook/2024/infections-diseases/hepatitis-a

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Hepatitis A Dosing

- **Dosing:** Hepatitis A Vaccine, Inactivated (Havrix®, VAQTA®)
  - Single dose IM before departure
  - Routine vaccination: 2-dose series given IM ≥ 6 months apart at age 12-23 months
  - Indicated at earlier age for travelers (6-11 months) but does not provide long-term protection
    - Must repeat series after patient is 12 months old (routine vaccination schedule)

Nelson N, Weng M. Hepatitis A. Centers for Disease Control and Prevention. May 1, 2023. Accessed January 4, 2024. https://wwwnc.cdc.gov/travel/yellowbook/2024/infections-diseases/hepatitis-a

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Vaccines for Blood-Borne Pathogens

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Hepatitis B

- **Pathogen:** Hepatitis B virus
- **Transmission:** Contaminated blood, blood products, and other bodily fluids (e.g. semen)
- **Presentation:** Abdominal pain, anorexia, fatigue, fever, jaundice, joint pain, clay-colored stool, vomiting
  - Mortality of acute hepatitis B is 1%
  - Chronic infection leads to liver cirrhosis, HCC, or liver failure in 15-40%
- **Indications:** Unvaccinated, humanitarian aid workers, medical tourists, and expatriates
  - High prevalence in Africa and the western Pacific
- **Contraindications:** Hypersensitivity to yeast

Nelson N, Weng M. Hepatitis A. Centers for Disease Control and Prevention. May 1, 2023. Accessed January 4, 2024. https://wwwnc.cdc.gov/travel/yellowbook/2024/infections-diseases/hepatitis-b

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Hepatitis B Dosing

- **Products:**
  - Hepatitis B Vaccine (Recombinant) (Engerix-B®)
  - Hepatitis B Vaccine (Recombinant), Adjuvanted (Heplisav-B®)
  - Hepatitis B Vaccine (Recombinant), Adjuvanted (Recombivax HB®)
  - Hepatitis A & Hepatitis B (Recombinant) Vaccine (Twinrix®)
- **Dosing:**
  - Routine vaccination: Three-dose series given IM on month 0, 1, and 6 (Heplisav-B® is 2 doses ≥ 1 month apart)
  - Twinrix® can be on accelerated schedule: 3 doses at 0, 7, and 21-30 days, then booster at 12 months
  - One or two doses provides some protection
    - E.g. Engerix-B® data for age 16-65: Seroprotection rate of 79% after two doses and 96% after all three doses

•Harris A. Hepatitis B. Centers for Disease Control and Prevention. May 1, 2023. Accessed January 4, 2024. https://wwwnc.cdc.gov/travel/yellowbook/2024/infections-diseases/hepatitis-b
•ENGERIX-B [Hepatitis B Vaccine (Recombinant)] [package insert]. Durham, NC: GlaxoSmithKline Biological. 2023.

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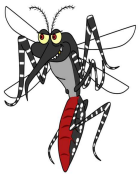
Vaccines for Mosquito-Borne Pathogens



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Japanese Encephalitis

- **Pathogen:** Japanese encephalitis virus, genus *Flavivirus*
- **Transmission:** Mosquito bite
- **Presentation:** Most infections asymptomatic, fever, headache, vomiting, < 1% develop neurologic disease, seizures, encephalitis, parkinsonian syndrome
  - Mortality 20-30% if patients who develop encephalitis
- **Indications:** Adventure tourists, long-term travelers (≥ 1 month), and expatriates
  - Endemicity: Asia and parts of the Western Pacific

Hills S, Lindsay N, Fischer M. Hepatitis B. Centers for Disease Control and Prevention. November 28, 2023. Accessed January 4, 2024. https://wwwnc.cdc.gov/travel/yellowbook/2024/infections-diseases/japanese-encephalitis

24

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Japanese Encephalitis Dosing

- **Dosing:** Japanese Encephalitis Vaccine, Inactivated, Adsorbed (Ixiaro®)
  - 2-dose series given IM 28 days apart, second dose at least one week before potential exposure
  - If at continued risk of exposure, can receive a booster (3rd dose) ≥ 1 year later

Hills S, Lindsay N, Fischer M. Hepatitis B. Centers for Disease Control and Prevention. November 28, 2023. Accessed January 4, 2024. https://wwwnc.cdc.gov/travel/yellowbook/2024/infections-diseases/japanese-encephalitis

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Yellow Fever

- **Pathogen:** Yellow fever virus, genus *Flavivirus*
- **Transmission:** Mosquito bite
- **Presentation:** Backache, chills, fever, myalgia, nausea, vomiting, prostration
  - Mortality 30-60% in severe cases
- **Indications:** Unvaccinated people visiting forested or savannah regions of endemic areas, or visiting locations with ongoing outbreaks
  - High endemicity: Sub-Saharan Africa, Tropical South America

Gershman M, Staples J. Yellow Fever. Centers for Disease Control and Prevention. May 1, 2023. Accessed January 4, 2024. https://wwwnc.cdc.gov/travel/yellowbook/2024/infections-diseases/yellow-fever

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Yellow Fever

- **Dosing:** Yellow Fever Vaccine (YF-Vax®)
  - 1 dose SubQ for age ≥ 9 months
- **Contraindication:** Severe allergic reaction to eggs, pregnant, or immunocompromised. Exceptions:
  - Asymptomatic HIV-infected adults with CD4 count ≥ 200 cells/mm^3
  - Asymptomatic HIV-infected children aged 9 months to 5 years with CD4 ≥ 15%

Gershman M, Staples J. Yellow Fever. Centers for Disease Control and Prevention. May 1, 2023. Accessed January 4, 2024. https://wwwnc.cdc.gov/travel/yellowbook/2024/infections-diseases/yellow-fever

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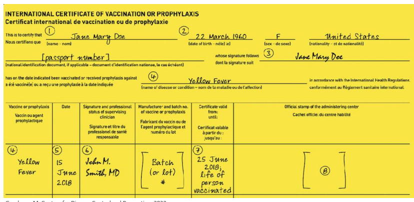
Yellow Fever Documentation

Live Vaccine!

- International Certificate of Vaccination or Prophylaxis (ICVP), required for proof of entry to some countries
- Valid 10 days after vaccination



INTERNATIONAL CERTIFICATE OF VACCINATION OR PROPHYLAXIS
Certificat international de vaccination ou de prophylaxie

This is to certify that / Nous certifions que ① Jane Mary Doe (name – nom) ② 22 March 1960 (date of birth – né(e) le) F (sex – de sexe) United States (nationality – et de nationalité)

[passport number] (national identification document, if applicable – document d'identification national, le cas échéant) whose signature follows / dont la signature suit ③ Jane Mary Doe

has on the date indicated been vaccinated or received prophylaxis against / a été vacciné(e) ou a reçu une prophylaxie à la date indiquée ④ Yellow Fever (name of disease or condition – nom de la maladie ou de l'affection) in accordance with the International Health Regulations. / conformément au Règlement sanitaire international.

Vaccine or prophylaxis / Vaccin ou agent prophylactique	Date	Signature and professional status of supervising clinician / Signature et titre du professionnel de santé responsable	Manufacturer and batch no. of vaccine or prophylaxis / Fabricant du vaccin ou de l'agent prophylactique et numéro du lot	Certificate valid from: until: / Certificat valable à partir du : jusqu'au :	Official stamp of the administering center / Cachet officiel du centre habilité
④ Yellow Fever	⑤ 15 June 2018	⑥ John M. Smith, MD	[Batch (or lot) #]	⑦ 25 June 2018; life of person vaccinated	[⑧]

Gershman M. Centers for Disease Control and Prevention. 2023.

Gershman M, Staples J. Yellow Fever. Centers for Disease Control and Prevention. May 1, 2023. Accessed January 4, 2024. https://wwwnc.cdc.gov/travel/yellowbook/2024/infections-diseases/yellow-fever

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Yellow Fever

Live Vaccine!

Table 5-25 Countries that require proof of yellow fever (YF) vaccination from all arriving travelers[1]

AFRICA		
Angola	Côte d'Ivoire	Niger
Benin	Democratic Republic of the Congo	Sierra Leone
Burkina Faso	Gabon	South Sudan
Burundi	Ghana	Togo
Cameroon	Guinea	Uganda
Central African Republic	Guinea-Bissau	
Congo, Republic of the	Mali	
THE AMERICAS		
French Guiana		

Gershman M. Centers for Disease Control and Prevention. 2023.

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Dengue

Live Vaccine!

- **Pathogen:** Dengue virus 1, 2, 3, and 4, genus *Flavivirus*
- **Transmission:** Mosquito bite
- **Presentation:** Asymptomatic (40-80%), acute febrile illness, ≤ 5% develop life-threatening disease: shock, respiratory distress, severe bleeding
  - Mortality up to 20% if untreated
- **Indications:** Previously tested positive for dengue infection and live in endemic areas, age 9-16 years
  - People at risk: All travelers, but increased risk for travelers on trips lasting > 6 months
  - Endemicity: Tropical and subtropical regions worldwide
  - Not for primary prevention or travelers just visiting an endemic area

Sanchez-Gonzalez L, Adams L, Paz-Bailey G. Dengue. Centers for Disease Control and Prevention. May 1, 2023. Accessed January 4, 2024. https://wwwnc.cdc.gov/travel/yellowbook/2024/infections-diseases/dengue

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Dengue

Live Vaccine!

- **Dosing:** Dengue Tetravalent Vaccine, Live (Dengvaxia®)
  - 3 doses SubQ at months 0, 6, and 12
- **Warning:** If patient has not already been infected, the vaccine can increase the risk for severe illness or hospitalization if infected after vaccination

Sanchez-Gonzalez L, Adams L, Paz-Bailey G. Dengue. Centers for Disease Control and Prevention. May 1, 2023. Accessed January 4, 2024. https://wwwnc.cdc.gov/travel/yellowbook/2024/infections-diseases/dengue

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Live Vaccine Considerations

- Must be administered ≥ 28 days apart if not given together
- If ≥ 2 live vaccines are given on separate days < 28 days apart, the second vaccine is invalid and must be repeated
- Interfere with tuberculin skin testing
  - Do tuberculin skin testing on the same day or ≥ 4 weeks later
- Contraindications: Pregnant or immunocompromised (high-level and low-level)

Kroger A, Freedman M. Vaccination & Immunoprophylaxis- General Principles. Centers for Disease Control and Prevention. May 1, 2023. Accessed January 4, 2024. https://wwwnc.cdc.gov/travel/yellowbook/2024/preparing/vaccination-and-immunoprophylaxis-general-principles

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High-Level Immunosuppression

- Receiving chemotherapy
- ≤ 2 months after solid organ transplantation
- Combined primary immunodeficiency disorder
- HIV infection with CD4 count < 200 cells/mm^3 for adults and < 15% CD4 in children
- Daily corticosteroid dose ≥ 20 mg of prednisone or equivalent for ≥ 14 days
- Receiving certain biologic immune modulators: Tumor necrosis factor-alpha blocker (TNF-α) or rituximab

Rubin LG, Levin MJ, Ljungman P, et al. 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host [published correction appears in Clin Infect Dis. 2014 Jul 1;59(1):144]. Clin Infect Dis. 2014;58(3):e44-e100. doi:10.1093/cid/cit684

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Low-Level Immunosuppression

- Asymptomatic HIV infection with CD4 count 200-499 cells/mm^3 for adults and 15-24% CD4 in children
- Daily corticosteroid dose < 20 mg or prednisone or equivalent for ≥ 14 days
- Alternate-day corticosteroid therapy
- Receiving methotrexate ≤ 0.4 mg/kg/week, azathioprine ≤ 3 mg/kg/day, or 6-mercaptopurine ≤ 1.5 mg/kg/day

Rubin LG, Levin MJ, Ljungman P, et al. 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host [published correction appears in Clin Infect Dis. 2014 Jul 1;59(1):144]. *Clin Infect Dis*. 2014;58(3):e44-e100. doi:10.1093/cid/cit684

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Live Vaccines

Live Vaccines	
Typhoid Fever	Vivotif®
Cholera	Vaxchora®
Yellow Fever	YF-VAX®
Dengue	Dengvaxia®

Kroger A, Freedman M. Vaccination & Immunoprophylaxis- General Principles. Centers for Disease Control and Prevention. May 1, 2023. Accessed January 4, 2024. https://wwwnc.cdc.gov/travel/yellowbook/2024/preparing/vaccination-and-immunoprophylaxis-general-principles.

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Inactivated Vaccines

Inactivated Vaccines	
Hepatitis A	Havrix®, VAQTA®
Hepatitis B	Engerix-B®, Heplisav-B®, Recombivax HB®
Hepatitis A and B	Twinrix®
Meningococcus	Menveo®, MenQuadfi®
Polio	IPOL®
Typhoid Fever	Typhim Vi®
Japanese Encephalitis	Ixiaro®

Kroger A, Freedman M. Vaccination & Immunoprophylaxis- General Principles. Centers for Disease Control and Prevention. May 1, 2023. Accessed January 4, 2024. https://wwwnc.cdc.gov/travel/yellowbook/2024/preparing/vaccination-and-immunoprophylaxis-general-principles.

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Concept Check

Which disease is spread by mosquitoes?

a. Hepatitis A
b. Dengue
c. Cholera
d. Typhoid Fever

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Concept Check

Which disease is spread by mosquitoes?

a. Hepatitis A
b. Dengue
c. Cholera
d. Typhoid Fever

Answer: Dengue

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How to Get Vaccinated

- Local health departments
  - Florida Department of Health
  - County health departments
- Travel medicine clinics
  - Many by appointment only
- Yellow fever special considerations
  - Must visit a Yellow Fever vaccine clinic
  - 147 clinics in Florida, 26 clinics in Dade County

Find a Clinic. Centers for Disease Control and Prevention. 2022.

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Concept Check

Which of the following is NOT a live vaccine?

a. YF-VAX®
b. Menveo®
c. Vivotif®
d. Vaxchora®

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Concept Check

Which of the following is NOT a live vaccine?

a. YF-VAX®
b. Menveo®
c. Vivotif®
d. Vaxchora®

Answer: Menveo®

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Travelers' Diarrhea

- The sudden onset of loose, frequent stools occurring while traveling

Travelers' Diarrhea Guideline Definitions	
Mild	Tolerable, not distressing, and does not interfere with planned activities
Moderate	Distressing or interferes with planned activities
Severe	Incapacitating or completely prevents planned activities; all dysentery (bloody stools) is considered severe
Persistent	Diarrhea lasting ≥ 2 weeks

Riddle MS, Connor BA, Beeching NJ, et al. Guidelines for the prevention and treatment of travelers' diarrhea: a graded expert panel report. J Travel Med. 2017;24(suppl_1):S57-S74. doi:10.1093/jtm/tax026

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Travelers' Diarrhea

- 10-70% of international travelers affected
- Cause most often bacterial: 80% of cases
  - *Escherichia coli* most common pathogen
  - *Campylobacter jejuni*
  - *Salmonella* species
  - *Shigella* species
- Viral pathogens: Norovirus

López-Vélez R, Lebens M, Bundy L, Barriga J, Steffen R. Bacterial travellers' diarrhoea: A narrative review of literature published over the past 10 years. Travel Med Infect Dis. 2022;47:102293. doi:10.1016/j.tmaid.2022.102293

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Risk Factors

- First month of travel
- Food: Prepared by street vendors, raw, not kept at safe temperature
- Using ice or non-bottled water
- Poor hygiene: Lack of hand washing or hand sanitizer
- Use of histamine blockers
- Chronic GI diseases (e.g. inflammatory bowel disease)

Conner B. Travelers' diarrhea: CDC Yellow Book 2024. Centers for Disease Control and Prevention. May 1, 2023. Accessed January 1, 2024. https://wwwnc.cdc.gov/travel/yellowbook/2024/preparing/travelers-diarrhea

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Travelers' Diarrhea Medications

Prevention	Treatment
Bismuth subsalicylate	Bismuth subsalicylate
Loperamide	Loperamide
Rifaximin	Azithromycin
	Fluoroquinolones
	Rifaximin

Conner B. Travelers' diarrhea: CDC Yellow Book 2024. Centers for Disease Control and Prevention. May 1, 2023. Accessed January 1, 2024. https://wwwnc.cdc.gov/travel/yellowbook/2024/preparing/travelers-diarrhea.

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Travelers' Diarrhea Prevention

- "Boil it, cook it, peel it, or forget it"
- Medical prophylaxis with bismuth subsalicylate (Pepto-Bismol®)
  - Dosing: 524 mg to 1050 mg by mouth four times daily (with meals and at bedtime)
  - Mechanism: Antisecretory activity (salicylate component) and antimicrobial activity (bismuth component)

•Conner B. Travelers' diarrhea: CDC Yellow Book 2024. Centers for Disease Control and Prevention. May 1, 2023. Accessed January 1, 2024. https://wwwnc.cdc.gov/travel/yellowbook/2024/preparing/travelers-diarrhea.
•Riddle MS, Connor BA, Beeching NJ, et al. Guidelines for the prevention and treatment of travelers' diarrhea: a graded expert panel report. J Travel Med. 2017;24(suppl_1):S57-S74. doi:10.1093/jtm/taw026
•Bismuth Subsalicylate. Lexi-Drugs. Lexicomp Online. Lexicomp, 2024. Updated January 1, 2024. Accessed January 2, 2024. http://online.lexi.com/.

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Travelers' Diarrhea Prevention

- Bismuth subsalicylate (Pepto-Bismol®)
  - Contraindications: Aspirin allergy, pregnant, renal insufficiency, gout, age < 3 years
  - CrCl < 50 mL/min: No dosage adjustment but use with caution (bismuth accumulation and salicylates can worsen renal function)
  - Caution in ≤ 12 years
  - Side effects: Black tongue, black stools, tinnitus, constipation, increased risk of bleeding

•Riddle MS, Connor BA, Beeching NJ, et al. Guidelines for the prevention and treatment of travelers' diarrhea: a graded expert panel report. J Travel Med. 2017;24(suppl_1):S57-S74. doi:10.1093/jtm/taw026
•Bismuth Subsalicylate. Lexi-Drugs. Lexicomp Online. Lexicomp, 2024. Updated January 1, 2024. Accessed January 2, 2024. http://online.lexi.com/.

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Travelers' Diarrhea Prevention

- Antibiotic prophylaxis should not be used by most travelers
  - Antibiotic resistance
  - Colonization with resistant bacteria
- When to give antibiotic prophylaxis:
  - Only for travelers at high risk of health-related complications of travelers' diarrhea
    - Serious chronic illness that predisposes patient to TD (e.g. achlorhydria, gastrectomy) or TD's complications (e.g., immunocompromised, diabetes, renal dysfunction)
    - Long-term morbidity after enteric infection (e.g. reactive arthritis, inflammatory bowel disease)

•Conner B. Travelers' diarrhea: CDC Yellow Book 2024. Centers for Disease Control and Prevention. May 1, 2023. Accessed January 1, 2024. https://wwwnc.cdc.gov/travel/yellowbook/2024/preparing/travelers-diarrhea.
•Riddle MS, Connor BA, Beeching NJ, et al. Guidelines for the prevention and treatment of travelers' diarrhea: a graded expert panel report. J Travel Med. 2017;24(suppl_1):S57-S74. doi:10.1093/jtm/taw026

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Travelers' Diarrhea Antibiotic Prophylaxis

- Rifaximin (Xifaxan®) preferred agent
  - Dosing: 200 mg one to three times daily (off-label)
  - Mechanism: Binds to bacterial DNA-dependent RNA polymerase, inhibiting bacterial RNA synthesis
  - Side effects: Nausea, peripheral edema, fatigue
    - Non-absorbable → safer agent
  - No renal dose adjustments
  - Limited data for patients < 12 years
- Fluoroquinolones not recommended

•Riddle MS, Connor BA, Beeching NJ, et al. Guidelines for the prevention and treatment of travelers' diarrhea: a graded expert panel report. J Travel Med. 2017;24(suppl_1):S57-S74. doi:10.1093/jtm/taw026
•Rifaximin. Lexi-Drugs. Lexicomp Online. Lexicomp, 2024. Updated December 5, 2023. Accessed January 2, 2024. http://online.lexi.com/

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Travelers' Diarrhea Treatment

- Hydration:
  - Increased fluid and salt intake
    - Moderate dehydration: 75 mL/kg in first 4 hours
  - Oral rehydration solution: Preferred if diarrhea or vomiting is prolonged
  - Add one packet to 1 L clean water
- Treatment approach based on travelers' diarrhea classification

PharmEasy. 2024.

Conner B. Travelers' diarrhea: CDC Yellow Book 2024. Centers for Disease Control and Prevention. May 1, 2023. Accessed January 1, 2024. https://wwwnc.cdc.gov/travel/yellowbook/2024/preparing/travelers-diarrhea.

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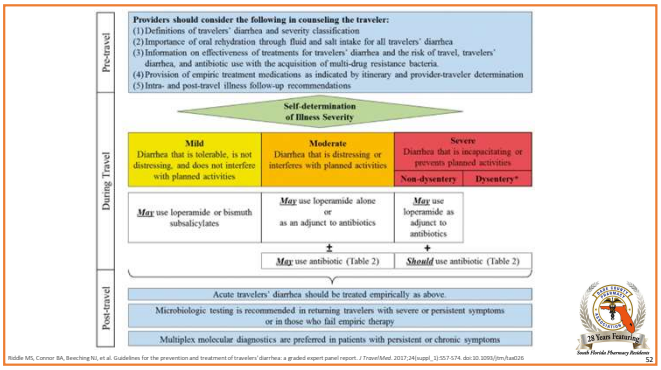

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Mild Travelers' Diarrhea

- Bismuth subsalicylate (Pepto-Bismol®):
  - Dosing: 524 mg to 1050 mg by mouth four times daily (with meals and at bedtime)
    - Same dosing as for prophylaxis
  - Maximum dose: 4,200 mg/24 hr

Mild
Diarrhea that is tolerable, is not distressing, and does not interfere with planned activities

May use loperamide or bismuth subsalicylates

Riddle MS. J Travel Med. 2017.

18 Years Training
South Florida Pharmacy Residency
Riddle MS, Connor BA, Beeching NJ, et al. Guidelines for the prevention and treatment of travelers' diarrhea: a graded expert panel report. J Travel Med. 2017;24(suppl_1):S57-S74. doi:10.1093/jtm/tax026
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Mild Travelers' Diarrhea

- Loperamide (Imodium®):
  - Dosing: 4 mg after first loose stool, 2 mg after each subsequent loose stool
    - Maximum dose of 16 mg/day (Rx) or 8 mg/day (OTC)
  - Mechanism:
    - Peripherally-acting opioid receptor agonist
    - ↓ intestinal peristalsis by decreasing acetylcholine and prostaglandin release
  - Duration: Up to two days

Mild
Diarrhea that is tolerable, is not distressing, and does not interfere with planned activities

May use loperamide or bismuth subsalicylates

Riddle MS. J Travel Med. 2017.

18 Years Training
South Florida Pharmacy Residency
•Loperamide (package insert). Bridgewater, NJ: Janssen Pharmaceutica Inc. https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/017009s005lbl.pdf. Published September 1996. Accessed January 1, 2024.
•Riddle MS, Connor BA, Beeching NJ, et al. Guidelines for the prevention and treatment of travelers' diarrhea: a graded expert panel report. J Travel Med. 2017;24(suppl_1):S57-S74. doi:10.1093/jtm/tax026
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Mild Travelers' Diarrhea

- Loperamide (Imodium®):
  - Black box warnings:
    - Torsades de pointes, cardiac arrest, and death reported when using higher than recommended dosages
    - Contraindicated in < 2 years
  - Contraindication: Dysentery (blood in stools, may have fever)
  - Counseling points:
    - Contact doctor if you see blood in your stools
    - May take with or without food
    - May cause abdominal cramps

Mild
Diarrhea that is tolerable, is not distressing, and does not interfere with planned activities
May use loperamide or bismuth subsalicylates

Riddle MS. *J Travel Med*. 2017.

•Loperamide [package insert]. Bridgewater, NJ: Janssen Pharmaceutica Inc. https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/017699s005lbl.pdf. Published September 1996. Accessed January 1, 2024.
•Riddle MS, Connor BA, Beeching NJ, et al. Guidelines for the prevention and treatment of travelers' diarrhea: a graded expert panel report. *J Travel Med*. 2017;24(suppl_1):S57-S74. doi:10.1093/jtm/tax026

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Moderate and Severe Travelers' Diarrhea

- Moderate TD Antibiotics:
  - Azithromycin or a fluoroquinolone
  - Rifaximin is an alternative
- Severe TD Antibiotics:
  - Azithromycin preferred
  - Fluoroquinolones or rifaximin are alternatives

Moderate	Severe	
Diarrhea that is distressing or interferes with planned activities	Diarrhea that is incapacitating or prevents planned activities	
	Non-dysentery	Dysentery*
May use loperamide alone or as an adjunct to antibiotics	***May*** use loperamide as adjunct to antibiotics	
±	+	
May use antibiotic (Table 2)	***Should*** use antibiotic (Table 2)	

Riddle MS. *J Travel Med*. 2017.

Riddle MS, Connor BA, Beeching NJ, et al. Guidelines for the prevention and treatment of travelers' diarrhea: a graded expert panel report. *J Travel Med*. 2017;24(suppl_1):S57-S74. doi:10.1093/jtm/tax026

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Antibiotic Counseling Points

- Azithromycin
  - Take with food to decrease GI discomfort (nausea and cramping)
  - Ototoxicity
  - QTc prolongation

Acute diarrhea antibiotic treatment recommendations

Antibiotic[a]	Dose	Treatment duration
Azithromycin[c,d]	1000 mg by mouth or	Single or 1-day divided[b]
	500 mg by mouth	3 day course
Levofloxacin	500 mg by mouth	Single dose[b] or 3 day course
Ciprofloxacin	750 mg by mouth or	Single dose[b]
	500 mg by mouth	3 day course
Ofloxacin	400 mg by mouth	Single dose[b] or 3 day course
Rifaximin[e]	200 mg by mouth three times daily	3 days

Riddle MS. *J Travel Med*. 2017.

Riddle MS, Connor BA, Beeching NJ, et al. Guidelines for the prevention and treatment of travelers' diarrhea: a graded expert panel report. *J Travel Med*. 2017;24(suppl_1):S57-S74. doi:10.1093/jtm/tax026

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Antibiotic Counseling Points

- Fluoroquinolones
  - ↓ GI upset = take with food
  - Take this medication 2 hours before or 6 hours after antacids, dairy, multivitamins, calcium, iron, and zinc
  - Increases sun sensitivity for up to 48 hours after treatment. Use sunscreen
  - QTc prolongation
  - Tendon rupture
  - CNS side effects: confusion, dizziness
  - Taste disturbances

Acute diarrhea antibiotic treatment recommendations

Antibiotic*	Dose	Treatment duration
Azithromycin[c,d]	1000 mg by mouth or	Single or 1-day divided[b]
	500 mg by mouth	3 day course
Levofloxacin	500 mg by mouth	Single dose[b] or 3 day course
Ciprofloxacin	750 mg by mouth or	Single dose[b]
	500 mg by mouth	3 day course
Ofloxacin	400 mg by mouth	Single dose[b] or 3 day course
Rifaximin[e]	200 mg by mouth three times daily	3 days

Riddle MS. J Travel Med. 2017.

Riddle MS, Connor BA, Beeching NJ, et al. Guidelines for the prevention and treatment of travelers' diarrhea: a graded expert panel report. J Travel Med. 2017;24(suppl_1):S57-S74. doi:10.1093/jtm/tax026

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When to Seek Medical Assistance

- Bloody diarrhea
- Diarrhea and high fever (> 102°F/38.9°C)
- Ongoing vomiting
- Symptoms lasting more than a few days
- Severe dehydration
  - Dry mouth
  - Decreased urine output
  - Muscle cramps
  - Dizziness

Riddle MS, Connor BA, Beeching NJ, et al. Guidelines for the prevention and treatment of travelers' diarrhea: a graded expert panel report. J Travel Med. 2017;24(suppl_1):S57-S74. doi:10.1093/jtm/tax026

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Concept Check

True or false, antibiotic prophylaxis should be used by most travelers to prevent travelers' diarrhea?

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Concept Check

True or false, antibiotic prophylaxis should be used by most travelers to prevent travelers' diarrhea?

Answer: False

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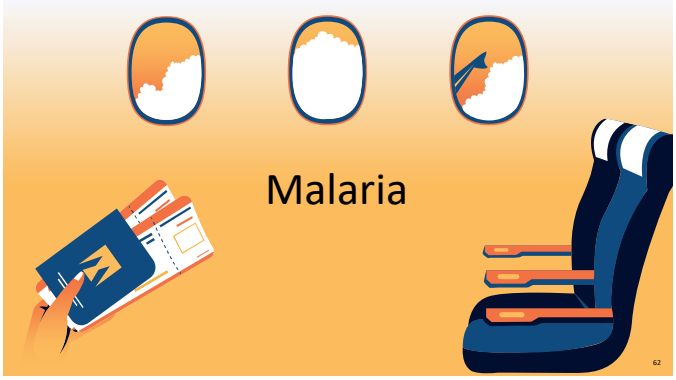

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Malaria

- Mosquito-borne disease caused by protozoan parasites: *Plasmodium falciparum, P. malariae, P. ovale,* and *P. vivax*
- WHO 2019 report = 228 million infections and 405,000 deaths
- In humans, it multiplies in liver then moves to red blood cells, destroying them
- Symptoms: Chills, headache, myalgias, malaise
  - Severe: AKI, acute respiratory distress syndrome, confusion, seizures, coma, death

Tan K, Abanyie F. Malaria. Centers for Disease Control and Prevention. May 1, 2023. Accessed January 4, 2024. https://wwwnc.cdc.gov/travel/yellowbook/2024/infections-diseases/malaria

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Malaria

- Endemicity: Africa, the Americas, and Asia
- Patients most at risk: Children, long-term travelers and expatriates, pregnant travelers, tourists, business travelers, missionaries, and visiting friends and relatives in areas with malaria

Tan K, Abanyie F. Malaria. Centers for Disease Control and Prevention. May 1, 2023. Accessed January 4, 2024. https://wwwnc.cdc.gov/travel/yellowbook/2024/infections-diseases/malaria

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Malaria Prevention

- Mosquito avoidance:
  - Stay in enclosed, air-conditioned rooms during dawn and dusk
  - Mosquito nets
  - Insecticide spray (e.g. DEET) or mosquito coils
  - Permethrin applied to mosquito nets and clothing
  - Long clothes

Tan K, Abanyie F. Malaria. Centers for Disease Control and Prevention. May 1, 2023. Accessed January 4, 2024. https://wwwnc.cdc.gov/travel/yellowbook/2024/infections-diseases/malaria

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Malaria Prevention Chemoprophylaxis

- Take medication before, during, and after travel to endemic area
- Consider patient-specific factors:
  - Pregnant or breastfeeding
  - Age
  - Length of time before travel
  - G6PD deficiency
  - Renal function
  - Visual changes
  - Arrhythmias
  - Seizures

Tan K, Abanyie F. Malaria. Centers for Disease Control and Prevention. May 1, 2023. Accessed January 4, 2024. https://wwwnc.cdc.gov/travel/yellowbook/2024/infections-diseases/malaria

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Prophylaxis Started 1-2 Days Prior to Travel

Medication	Adult Dose	Dosing Information	Precautions/ Contraindications/Notes
Atovaquone/Proguanil (Malarone®)	250 mg/100 mg PO once daily	Stop one week after travel	• CI: CrCl < 30 mL/min • Not recommended: Pregnant, breastfeeding • Nausea, take with food or milk
Doxycycline (Vibramycin®)	100 mg PO once daily	Stop four weeks after travel	• CI: < 8 years, pregnant, breastfeeding • Photosensitivity • Nausea, take with food or milk • Preferred in camping (prevents rickettsial infections and leptospirosis)
Primaquine	30 mg PO once daily	Stop one week after travel	• CI: Pregnant, breastfeeding • Avoid in G6PD deficiency

Tan K, Abanyie F. Malaria. Centers for Disease Control and Prevention. May 1, 2023. Accessed January 4, 2024. https://wwwnc.cdc.gov/travel/yellowbook/2024/infections-diseases/malaria

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Prophylaxis Started 1-2 Weeks Prior to Travel

Medication	Adult Dose	Dosing Information	Precautions/ Contraindications/Notes
Chloroquine	500 mg PO once weekly	• Start 1-2 weeks before travel • Stop 4 weeks after travel	• CI: Underlying retinal/visual changes • Retinal toxicity/visual changes • Avoid if area has resistance • Safe in children, pregnancy
Mefloquine	250 mg PO once weekly	• Start ≥ 2 weeks before travel • Stop 4 weeks after travel	• CI: Underlying psychiatric conditions, seizures, arrhythmias • Avoid if area has resistance • Safe in children, pregnancy, breastfeeding
Tafenoquine (Arakoda®, Krintafel®)	200 mg PO once daily for 3 days, then 200 mg PO once weekly starting one week after last loading dose	• Start loading dose 3 days before travel • Stop 1 week after travel • Can use for up to 6 months	• CI: Underlying psychiatric conditions • Avoid in G6PD deficiency, pregnancy, breastfeeding

Tan K, Abanyie F. Malaria. Centers for Disease Control and Prevention. May 1, 2023. Accessed January 4, 2024. https://wwwnc.cdc.gov/travel/yellowbook/2024/infections-diseases/malaria

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Malaria Treatment

- CDC has recommendations for malaria treatment
- Treatment medication depends on *Plasmodium* species and if located in area with chloroquine or mefloquine resistance
- Travel medicine concerns: Patients may choose to carry a "reliable supply" of medication in case of malaria diagnosis

Tan K, Abanyie F. Malaria. Centers for Disease Control and Prevention. May 1, 2023. Accessed January 4, 2024. https://wwwnc.cdc.gov/travel/yellowbook/2024/infections-diseases/malaria

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Travel Health Concerns

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Pre-Travel Preparation

≥ 1 month before trip:

- ☑ Vaccinations
- ☑ Travel insurance
  - Travel health insurance and medical evacuation insurance
  - May chose short-term supplemental policy
- ☑ Review CDC's Travelers' Health website

One week before trip:

- ☑ Pack medications
- ☑ Pack a health kit
- ☑ Pack copies of prescriptions and important health documents
- ☑ Download the CDC phone application
- ☑ Enroll in STEP

Travelers' health. Centers for Disease Control and Prevention. Updated 2023. Accessed January 4, 2024. https://wwwnc.cdc.gov/travel/.

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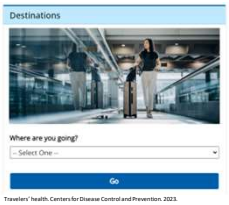
CDC Travelers' Health

- Destinations: Personalized recommendations based on travel destination
  - Travel health notices
  - Vaccines and medications
  - Non-vaccine-preventable diseases
  - Tips to stay healthy and safe
  - Personalized medical packing list
- CDC Yellow Book: Made for clinicians
  - Current travel health guidelines
  - Vaccine recommendations
  - Maps, tables, and charts



Travelers' health. Centers for Disease Control and Prevention. Updated 2023. Accessed January 4, 2024. https://wwwnc.cdc.gov/travel/.

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Global TravEpiNet

Heading Home Healthy

A program to help travelers stay healthy when they are returning home to visit friends and relatives

Travelers' Rapid Health Information Portal

Health advice for safe travel based on the recommendations of the U.S. Centers for Disease Control and Prevention

Pre-Travel Providers' Rapid Evaluation Portal

An interactive tool that guides you through preparing a U.S. traveler for a safe and healthy international trip

- Nationwide consortium of travel clinics supported by CDC

Global TravEpiNet. Global TravEpiNet - Massachusetts General Hospital. August 18, 2023. Accessed January 4, 2024. https://gten.massgeneral.org/.

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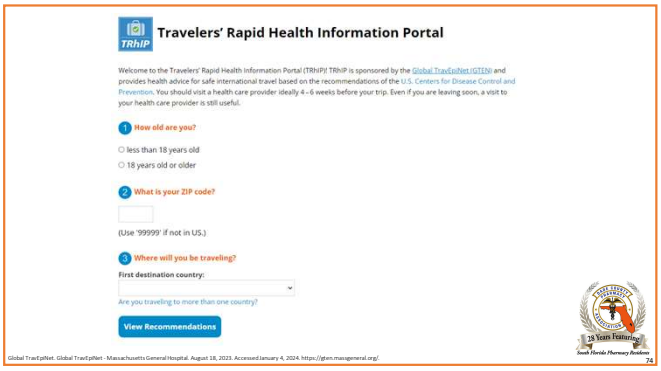

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Packing a Health Kit

Prescription Medications	• Keep medication in original containers in carry-on luggage • Insulin, inhalers, epinephrine auto-injectors
OTC Medications	• Antacids • Pain medication • Cough suppressants • Decongestants • Sleep aid • Saline nose spray • Mild laxatives • Anti-diarrheals
Travel Medications	• Travelers' diarrhea prophylaxis • Altitude sickness medication
Other Supplies	• Water purification tablets • Insect repellent • Permethrin clothing spray • Bandages • Medical alert bracelet • Hand sanitizer

Travelers' health. Centers for Disease Control and Prevention. Updated 2023. Accessed January 4, 2024. https://wwwnc.cdc.gov/travel/.

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New Developments in Travel Medicine

- CDC's Travel Health Notices page includes important information for travelers and is regularly updated
  - Global health risks during outbreaks, special events, and natural disasters
  - Sporadic cases of disease in new location
  - Advice on preventing infection or adverse health effects

	Travel Health Notices
Level 4	Avoid all travel
Level 3	Reconsider nonessential travel
Level 2	Practice enhanced precautions
Level 1	Practice usual precautions

Travel health notices. Centers for Disease Control and Prevention. December 21, 2023. Accessed January 4, 2024. https://wwwnc.cdc.gov/travel/notices.

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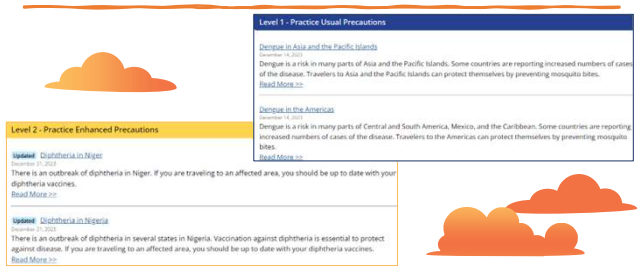
New Developments in Travel Medicine



Travel health notices. Centers for Disease Control and Prevention. December 21, 2023. Accessed January 4, 2024. https://wwwnc.cdc.gov/travel/notices.

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New Developments in Travel Medicine

- CDC's Traveler-Based Genomic Surveillance (TGS) program
  - Anonymously collects nasal swab samples from volunteer international travelers arriving at U.S. airports
  - Tracks emergence of new and potentially significant SARS-CoV-2 variants, most recently, BA.2.86
  - Samples shared with CDC's laboratory → viral characterization to learn about variant's transmissibility, virulence, and response to current treatments or vaccines
  - Started in 2021 for SARS-CoV-2 alone, now expanded
    - For this respiratory season, TGS is completing a multipathogen pilot testing for Flu A/B, RSV, SARS-CoV-2

Traveler-based genomic surveillance for early detection of new SARS-COV-2 variants. Centers for Disease Control and Prevention. October 27, 2023. Accessed January 9, 2024. https://wwwnc.cdc.gov/travel/page/travel-genomic-surveillance.

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Case Example

Patient CS is a 21 YO M who just graduated, and to celebrate he is planning an international backing trip with his friends. He knows there are special vaccines and travel considerations to keep in mind, but he has never left the country before. He comes to you, his pharmacist, for advice. What will you do to help CS?

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Case Example

- Ask CS for more information about his trip
  - What countries will he visit
  - How long is the trip
  - What type of activities will he partake in

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Case Example

- Ask CS for more information about his trip
  - What countries will he visit:
    Starting in Cusco, Peru, then traveling to La Paz, Bolivia
  - How long is the trip:
    Two weeks
  - What type of activities will he partake in:
    Hiking, camping outdoors

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Case Example

- Start with the CDC destinations website

Travelers' health. Centers for Disease Control and Prevention. 2023.

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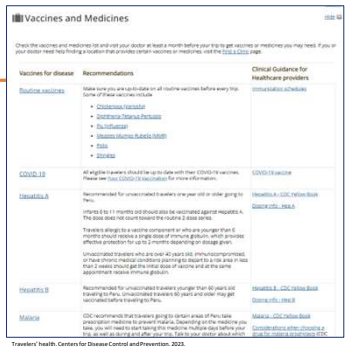
Case Example

- Vaccines needed:
  - Hepatitis A, hepatitis B, rabies, typhoid
- Yellow Fever:
  - Bolivia requires vaccination for entry only if arriving from high-risk countries, so not needed for CS



Travelers' health. Centers for Disease Control and Prevention. 2023.

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Case Example

- Malaria:
  - Only recommended for travel limited to areas < 7,550 feet elevation in Peru and Bolivia, so not needed for CS

Travelers' health. Centers for Disease Control and Prevention. 2023.

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Final Travel Tips

Mosquito Bite Prevention	Safe Food and Drinks	Hand Hygiene

• Insect repellent
  • DEET, picaridin
• Loose-fitting, long clothing
  • Treat with permethrin spray
• Use screens, mosquito nets
	• Safe:
	  • Served hot
	  • Dry, pre-packaged
	  • Fruit with peels
	  • Bottled or canned
	• Not safe:
	  • Raw
	  • Street food
		• Wash hands often with soap and water for ≥ 20 seconds
		• Alternative is hand sanitizer with ≥ 60% alcohol

• Prevent Mosquito Bites. Centers for Disease Control and Prevention. August 17, 2023. Accessed January 4, 2024. https://www.cdc.gov/mosquitoes/mosquito-bites/prevent-mosquito-bites.html.
• Travelers' health. Centers for Disease Control and Prevention. Updated 2023. Accessed January 4, 2024. https://wwwnc.cdc.gov/travel/

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Summary

- Many vaccines specific to travelers, with different vaccine recommendations based on travel location
- Travelers' diarrhea and malaria are both preventable, but if a patient gets either, there are multiple treatment options
- Many resources available for travel health information, news, and updates for patients and clinicians

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Thank you!

Questions?

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Travel Medicine Made Plane & Simple

Megan Backus, Pharm.D.
Baptist Health - Boca Raton Regional Hospital
January 21, 2024

89

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Updates on Pharmacist Vaccinating the Public

Lyreima Valentin Acevedo, BS,PharmD
Walgreens and Nova Southeastern University COP
Miami, Florida
January 21,2024

1

1

Objectives

- Describe recent updates on vaccines and pharmacists' immunization authority in Florida
- Determine immunization patient eligibility in adults
- Identify reliable sources for pharmacists on vaccines updates

2

Florida Statutes

3

According to Florida Statutes Pharmacists can administer:

- Immunizations or vaccines listed in the Adult Immunization Schedule as of March 31, 2022, by the United States Centers for Disease Control and Prevention
- Immunizations or vaccines recommended by the United States Centers for Disease Control and Prevention for international travel as of March 31, 2022

4

According to Florida Statutes Pharmacists can administer:

- Immunizations or vaccines licensed for use in the United States, or which have been authorized for emergency use, by the United States Food and Drug Administration as of March 31, 2022
- Immunizations or vaccines approved by the board in response to a state of emergency declared by the Governor pursuant to s. 252.36

5

COVID-19 & Flu Vaccine

- Immunizations in Florida are only administered under protocol with the exception of COVID-19 and Flu vaccines

6

Epinephrine

- In order to address any unforeseen allergic reaction, a pharmacist may administer epinephrine using an autoinjector delivery system within the framework of an established protocol under a supervising physician licensed under chapter 458 or chapter 459

7

Pharmacist Training

- Must complete an immunization administration certification program of no fewer than 20 hours, approved by the Florida Board of Pharmacy
- 3-hour immunization continuing education (CE) course

8

Immunization Eligibility in Adults

9

Flu Vaccine

10

Types of Flu Vaccines

- Fluzone Quadrivalent vaccine
- Fluzone High-Dose Quadrivalent vaccine
- Fluad Quadrivalent vaccine
- Fluad High-Dose Quadrivalent vaccine
- Fluarix Quadrivalent vaccine
- Flulaval Quadrivalent vaccine
- Afluria Quadrivalent vaccine

11

Flu Vaccine Eligibility and Schedule

- Age 3 years or older: 1 dose of any influenza vaccine appropriate for age and health status annually.
- Age 65 years or older: Any one of the quadrivalent high-dose inactivated influenza vaccine

12

COVID-19 Vaccine

13

Types of COVID-19 Vaccines

- Comirnaty Pfizer
- COVID-19 Pfizer Toddler
- COVID Pfizer Pediatric
- Spikevax Moderna
- COVID Moderna 3-11

14

COVID-19 Vaccine

- Everyone aged 5 years and older should get 1 dose of an updated COVID-19 vaccine to protect against serious illness from COVID-19
- Children aged 6 months–4 years need multiple doses of COVID-19 vaccines to be up to date, including at least 1 dose of updated COVID-19 vaccine
- People who are moderately or severely immunocompromised may get additional doses of updated COVID-19 vaccine

15

COVID-19 Vaccine Eligibility

16

Moderna

17

COVID-19 CDC Updated 2023-2024 Formula- Moderna

Table 1a. For people who are **NOT** moderately or severely immunocompromised*

2023-24 Moderna COVID-19 Vaccine
Vaccine type: mRNA - Do **NOT** use any previously available Moderna COVID-19 vaccine products.

Age	COVID-19 Vaccination History† (regardless of COVID-19 vaccine formula)	2023-24 Vaccine Schedule	Administer
6 months through 4 years	Unvaccinated (0 doses)	Give a 2-dose initial series. Administer: • Dose 1 now • Dose 2 at least 4–8 weeks after Dose 1§	0.25 mL/25 µg From single-dose vial with dark blue cap and green label Intramuscular (IM) injection
	1 previous dose of any Moderna COVID-19 Vaccine (Dose 1)§	Give Dose 2 at least 4–8 weeks after the last dose§	
	2 or more doses Moderna COVID-19 Vaccine, **NOT** including at least 1 dose of 2023–24 vaccine¶¶	Give 1 dose at least 8 weeks (2 months) after the last dose	
	2 or more doses Moderna COVID-19 Vaccine, **INCLUDING** at least 1 dose of 2023–24) vaccine¶¶	No further doses are indicated	
5 through 11 years	Unvaccinated (0 doses)	Give 1 dose now	0.25 mL/25 µg From single-dose vial with dark blue cap and green label Intramuscular (IM) injection
	Any number of previous doses COVID-19 vaccine, **NOT** including at least 1 dose of 2023–24 vaccine	Give 1 dose at least 8 weeks (2 months) after the last dose	
	Any number of previous doses COVID-19 vaccine, **INCLUDING** at least 1 dose of 2023–24 vaccine	No further doses are indicated	

COVID-19 Vaccine. https://www.cdc.gov/vaccines/covid-19/downloads/COVID-19-immunization-schedule-ages-6months-older.pdf

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COVID-19 CDC Updated 2023-2024 Formula-Moderna

Table 1a. For people who are **NOT** moderately or severely immunocompromised[†]

2023-24 Moderna COVID-19 Vaccine Vaccine type: mRNA - Do **NOT** use any previously available Moderna COVID-19 vaccine products.			
12 years and older	Unvaccinated (0 doses)	Give 1 dose now	0.5 mL/50 µg From single-dose vial with dark blue cap and blue label Intramuscular (IM) injection
	Any number of previous doses COVID-19 vaccine, **NOT** including at least 1 dose of 2023–24 vaccine	Give 1 dose at least 8 weeks (2 months) after the previous dose	
	Any number of previous doses COVID-19 vaccine, **INCLUDING** at least 1 dose of 2023–24 vaccine	No further doses are indicated	

COVID-19 Vaccine. https://www.cdc.gov/vaccines/covid-19/downloads/COVID-19-immunization-schedule-ages-6months-older.pdf

19

Pfizer

20

COVID-19 CDC Updated 2023-2024 Formula-Pfizer

Table 1b. For people who are **NOT** moderately or severely immunocompromised[†]

2023-24 Pfizer-BioNTech COVID-19 Vaccine Vaccine type: mRNA - Do **NOT** use any previously available Pfizer-BioNTech COVID-19 vaccine products.			
Age	COVID-19 Vaccination History[†] (regardless of COVID-19 vaccine formula)	2023-24 Vaccine Schedule	Administer
6 months through 4 years	Unvaccinated (0 doses)	Give a 3-dose initial series. Administer: • Dose 1 now • Dose 2 at least 3–8 weeks after Dose 1[*] • Dose 3 at least 8 weeks (2 months) after Dose 2	0.2 mL/3 µg From yellow-capped vial with yellow label Intramuscular (IM) injection
	1 previous dose of any Pfizer-BioNTech COVID-19 Vaccine (Dose 1)[*]	Complete series. Administer: • Dose 2 at least 3–8 weeks after Dose 1[*] • Dose 3 at least 8 weeks (2 months) after Dose 2	
	2 doses of any Pfizer-BioNTech COVID-19 Vaccine (Doses 1 and 2)[*§]	Complete series. Administer: • Dose 3 at least 8 weeks (2 months) after Dose 2	
	3 or more doses Pfizer-BioNTech COVID-19 Vaccine, **NOT** including at least 1 dose of 2023–24 COVID-19 vaccine[¶]	Give 1 dose at least 8 weeks (2 months) after the last dose	
	3 or more doses Pfizer-BioNTech COVID-19 Vaccine, **INCLUDING** at least 1 dose of 2023–24 COVID-19 vaccine[¶]	No further doses are indicated	
5 through 11 years	Unvaccinated (0 doses)	Give 1 dose now	0.3 mL/10 µg From blue-capped vial with blue label Intramuscular (IM) injection
	Any number of previous doses COVID-19 vaccine, **NOT** including at least 1 dose of 2023–24 COVID-19 vaccine	Give 1 dose at least 8 weeks (2 months) after the last dose	
	Any number of previous doses COVID-19 vaccine, **INCLUDING** at least 1 dose of 2023–24 COVID-19 vaccine	No further doses are indicated	

COVID-19 Vaccine. https://www.cdc.gov/vaccines/covid-19/downloads/COVID-19-immunization-schedule-ages-6months-older.pdf

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COVID-19 CDC Updated 2023-2024 Formula- Pfizer

Table 1b. For people who are **NOT** moderately or severely immunocompromised*

2023-24 Pfizer-BioNTech COVID-19 Vaccine
Vaccine type: mRNA - Do **NOT** use any previously available Pfizer-BioNTech COVID-19 vaccine products.

Age	COVID-19 Vaccination History† (regardless of COVID-19 vaccine formula)	2023-24 Vaccine Schedule	Administer
12 years and older	Unvaccinated (0 doses)	Give 1 dose now	0.3 mL/30 µg From gray-capped vial with gray label or manufacturer-filled syringe with gray box on label Intramuscular (IM) injection
	Any number of previous doses COVID-19 vaccine, **NOT** including at least 1 dose of 2023-24 COVID-19 vaccine	Give 1 dose at least 8 weeks (2 months) after the last dose	
	Any number of previous doses COVID-19 vaccine, **INCLUDING** at least 1 dose of 2023-24 COVID-19 vaccine	No further doses are indicated	

COVID-19 Vaccine. https://www.cdc.gov/vaccines/covid-19/downloads/COVID-19-immunization-schedule-ages-6months-older.pdf

22

Moderna-Immunocompromised

23

COVID-19 CDC Updated 2023-2024 Formula-Moderna

Table 2a. For people who **ARE** moderately or severely immunocompromised

2023-24 Moderna COVID-19 Vaccine
Vaccine type: mRNA - Do **NOT** use any previously available Moderna COVID-19 vaccine products.

Age	COVID-19 Vaccination History† (regardless of COVID-19 vaccine formula)	2023-24 Vaccine Schedule	Administer
6 months through 4 years	Unvaccinated (0 doses)	Give a 3-dose initial series. Administer: • Dose 1 now • Dose 2 at least 4 weeks after Dose 1 • Dose 3 at least 4 weeks after Dose 2	0.25 mL/25 µg From single-dose vial with dark blue cap and green label Intramuscular (IM) injection
	1 previous dose of any Moderna COVID-19 Vaccine (Dose 1)‡	Complete series. Administer: • Dose 2 at least 4 weeks after Dose 1 • Dose 3 at least 4 weeks after Dose 2	
	2 doses of any Moderna COVID-19 Vaccine (Doses 1 and 2)‡§	Complete series. Administer: • Dose 3 at least 4 weeks after Dose 2	
	3 or more doses of Moderna COVID-19 Vaccine, **NOT** including at least 1 dose of 2023-24 COVID-19 vaccine‡	Give 1 dose at least 8 weeks (2 months) after the previous dose	
	3 or more doses of Moderna COVID-19 Vaccine, **INCLUDING** at least 1 dose of 2023-24 COVID-19 vaccine‡	People who are moderately or severely immunocompromised have the **option to receive 1 additional dose at least 8 weeks (2 months) following** the last recommended dose. Further additional dose(s) may be administered, **informed by the clinical judgement** of a healthcare provider and personal preference and circumstances. Any further additional doses should be administered at **least 8 weeks (2 months) after the last** COVID-19 vaccine dose.	

COVID-19 Vaccine. https://www.cdc.gov/vaccines/covid-19/downloads/COVID-19-immunization-schedule-ages-6months-older.pdf

24

COVID-19
Updated 2023-2024 Formula-Moderna

Table 2a. For people who **ARE** moderately or severely immunocompromised

2023-24 Moderna COVID-19 Vaccine
Vaccine type: mRNA - Do **NOT** use any previously available Moderna COVID-19 vaccine products.

Age	COVID-19 Vaccination History[1] (regardless of COVID-19 vaccine formula)	2023-24 Vaccine Schedule	Administer
5 through 11 years	Unvaccinated (0 doses)	Give a 3-dose initial series. Administer: • Dose 1 now • Dose 2 at least 4 weeks after Dose 1 • Dose 3 at least 4 weeks after Dose 2	0.25 mL/25 µg From single-dose vial with dark blue cap and green label Intramuscular (IM) injection
	1 previous dose of any Moderna COVID-19 Vaccine (Dose 1)[2]	Complete series. Administer: • Dose 2 at least 4 weeks after Dose 1 • Dose 3 at least 4 weeks after Dose 2	
	2 doses of any Moderna COVID-19 Vaccine (Doses 1 and 2)[2]	Complete series. Administer: • Dose 3 at least 4 weeks after Dose 2	
	3 or more doses of Moderna COVID-19 Vaccine, **NOT** including at least 1 dose of 2023–24 COVID-19 vaccine[3]	Give 1 dose at least 8 weeks (2 months) after the last dose	
	3 or more doses of Moderna COVID-19 Vaccine, **INCLUDING** at least 1 dose of 2023–24 COVID-19 vaccine[3]	People who are moderately or severely immunocompromised have the **option to receive 1 additional dose at least 8 weeks (2 months) following** the last recommended dose. Further additional dose(s) may be administered, **informed by the clinical judgement** of a healthcare provider and personal preference and circumstances. Any further additional doses should be administered at **least 8 weeks (2 months) after the last** COVID-19 vaccine dose.	

COVID-19 Vaccine. https://www.cdc.gov/vaccines/covid-19/downloads/COVID-19-immunization-schedule-ages-6months-older.pdf

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COVID-19 CDC
Updated 2023-2024 Formula-Moderna

Table 2a. For people who **ARE** moderately or severely immunocompromised *Continued*

2023-24 Moderna COVID-19 Vaccine - CONTINUED
Vaccine type: mRNA - Do **NOT** use any previously available Moderna COVID-19 vaccine products.

Age	COVID-19 Vaccination History[1] (regardless of COVID-19 vaccine formula)	2023-24 Vaccine Schedule	Administer
12 years and older	Unvaccinated (0 doses	Give a 3-dose initial series. Administer: • Dose 1 now • Dose 2 at least 4 weeks after Dose 1 • Dose 3 at least 4 weeks after Dose 2	0.5 mL/50 µg From single-dose vial with dark blue cap and blue label Intramuscular (IM) injection
	1 previous dose of any Moderna COVID-19 Vaccine (Dose 1)[2]	Complete series. Administer: • Dose 2 at least 4 weeks after Dose 1 • Dose 3 at least 4 weeks after Dose 2	
	2 doses of any Moderna COVID-19 Vaccine (Doses 1 and 2)[2]	Complete series. Administer: • Dose 3 at least 4 weeks after Dose 2	
	3 or more doses of Moderna COVID-19 Vaccine, **NOT** including at least 1 dose of 2023–24 COVID-19 vaccine[3]	Give 1 dose at least 8 weeks (2 months) after the previous dose	
	3 or more doses of Moderna COVID-19 Vaccine, **INCLUDING** at least 1 dose of 2023–24 COVID-19 vaccine[3]	People who are moderately or severely immunocompromised have the **option to receive 1 additional dose at least 8 weeks (2 months) following** the last recommended dose. Further additional dose(s) may be administered, **informed by the clinical judgement** of a healthcare provider and personal preference and circumstances. Any further additional doses should be administered at **least 8 weeks (2 months) after the last** COVID-19 vaccine dose.	

COVID-19 Vaccine. https://www.cdc.gov/vaccines/covid-19/downloads/COVID-19-immunization-schedule-ages-6months-older.pdf

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Pfizer-Immunocompromised

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COVID-19 CDC Updated 2023-2024 Formula-Pfizer

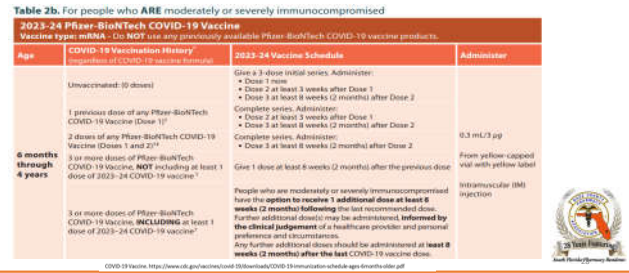

Table 2b. For people who **ARE** moderately or severely immunocompromised

2023-24 Pfizer-BioNTech COVID-19 Vaccine
Vaccine type: mRNA - Do **NOT** use any previously available Pfizer-BioNTech COVID-19 vaccine products.

Age	COVID-19 Vaccination History* (regardless of COVID-19 vaccine formula)	2023-24 Vaccine Schedule	Administer
6 months through 4 years	Unvaccinated: (0 doses)	Give a 3-dose initial series. Administer: • Dose 1 now • Dose 2 at least 3 weeks after Dose 1 • Dose 3 at least 8 weeks (2 months) after Dose 2	0.3 mL/3 µg From yellow-capped vial with yellow label Intramuscular (IM) injection
	1 previous dose of any Pfizer-BioNTech COVID-19 Vaccine (Dose 1)†	Complete series. Administer: • Dose 2 at least 3 weeks after Dose 1 • Dose 3 at least 8 weeks (2 months) after Dose 2	
	2 doses of any Pfizer-BioNTech COVID-19 Vaccine (Doses 1 and 2)†‡	Complete series. Administer: • Dose 3 at least 8 weeks (2 months) after Dose 2	
	3 or more doses of Pfizer-BioNTech COVID-19 Vaccine, **NOT** including at least 1 dose of 2023–24 COVID-19 vaccine†	Give 1 dose at least 8 weeks (2 months) after the previous dose	
	3 or more doses of Pfizer-BioNTech COVID-19 Vaccine, **INCLUDING** at least 1 dose of 2023–24 COVID-19 vaccine†	People who are moderately or severely immunocompromised have the **option to receive 1 additional dose at least 8 weeks (2 months) following** the last recommended dose. Further additional dose(s) may be administered, **informed by the clinical judgement** of a healthcare provider and personal preference and circumstances. Any further additional doses should be administered at **least 8 weeks (2 months) after the last** COVID-19 vaccine dose.	

COVID-19 Vaccine. https://www.cdc.gov/vaccines/covid-19/downloads/COVID-19-immunization-schedule-ages-6months-older.pdf

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COVID-19 CDC Updated 2023-2024 Formula-Pfizer

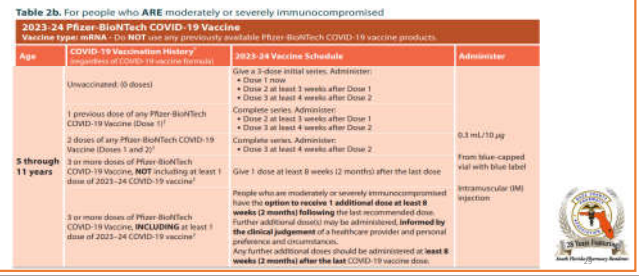

Table 2b. For people who **ARE** moderately or severely immunocompromised

2023-24 Pfizer-BioNTech COVID-19 Vaccine
Vaccine type: mRNA - Do **NOT** use any previously available Pfizer-BioNTech COVID-19 vaccine products.

Age	COVID-19 Vaccination History* (regardless of COVID-19 vaccine formula)	2023-24 Vaccine Schedule	Administer
5 through 11 years	Unvaccinated: (0 doses)	Give a 3-dose initial series. Administer: • Dose 1 now • Dose 2 at least 3 weeks after Dose 1 • Dose 3 at least 4 weeks after Dose 2	0.3 mL/10 µg From blue-capped vial with blue label Intramuscular (IM) injection
	1 previous dose of any Pfizer-BioNTech COVID-19 Vaccine (Dose 1)†	Complete series. Administer: • Dose 2 at least 3 weeks after Dose 1 • Dose 3 at least 4 weeks after Dose 2	
	2 doses of any Pfizer-BioNTech COVID-19 Vaccine (Doses 1 and 2)†	Complete series. Administer: • Dose 3 at least 4 weeks after Dose 2	
	3 or more doses of Pfizer-BioNTech COVID-19 Vaccine, **NOT** including at least 1 dose of 2023–24 COVID-19 vaccine†	Give 1 dose at least 8 weeks (2 months) after the last dose	
	3 or more doses of Pfizer-BioNTech COVID-19 Vaccine, **INCLUDING** at least 1 dose of 2023–24 COVID-19 vaccine†	People who are moderately or severely immunocompromised have the **option to receive 1 additional dose at least 8 weeks (2 months) following** the last recommended dose. Further additional dose(s) may be administered, **informed by the clinical judgement** of a healthcare provider and personal preference and circumstances. Any further additional doses should be administered at **least 8 weeks (2 months) after the last** COVID-19 vaccine dose.	

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COVID-19 CDC Updated 2023-2024 Formula-Pfizer

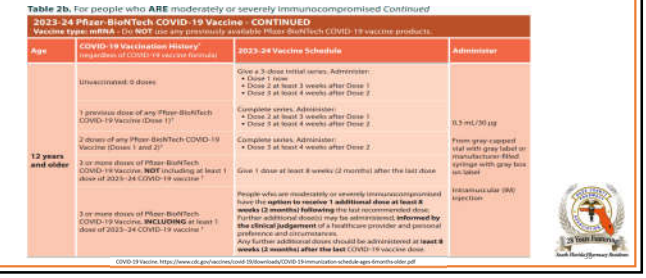

Table 2b. For people who **ARE** moderately or severely immunocompromised *Continued*

2023-24 Pfizer-BioNTech COVID-19 Vaccine - CONTINUED
Vaccine type: mRNA - Do **NOT** use any previously available Pfizer-BioNTech COVID-19 vaccine products.

Age	COVID-19 Vaccination History* (regardless of COVID-19 vaccine formula)	2023-24 Vaccine Schedule	Administer
12 years and older	Unvaccinated: 0 doses	Give a 3-dose initial series. Administer: • Dose 1 now • Dose 2 at least 3 weeks after Dose 1 • Dose 3 at least 4 weeks after Dose 2	0.3 mL/30 µg From gray-capped vial with gray label or manufacturer-filled syringe with gray box on label Intramuscular (IM) injection
	1 previous dose of any Pfizer-BioNTech COVID-19 Vaccine (Dose 1)†	Complete series. Administer: • Dose 2 at least 3 weeks after Dose 1 • Dose 3 at least 4 weeks after Dose 2	
	2 doses of any Pfizer-BioNTech COVID-19 Vaccine (Doses 1 and 2)†	Complete series. Administer: • Dose 3 at least 4 weeks after Dose 2	
	3 or more doses of Pfizer-BioNTech COVID-19 Vaccine, **NOT** including at least 1 dose of 2023–24 COVID-19 vaccine†	Give 1 dose at least 8 weeks (2 months) after the last dose	
	3 or more doses of Pfizer-BioNTech COVID-19 Vaccine, **INCLUDING** at least 1 dose of 2023–24 COVID-19 vaccine†	People who are moderately or severely immunocompromised have the **option to receive 1 additional dose at least 8 weeks (2 months) following** the last recommended dose. Further additional dose(s) may be administered, **informed by the clinical judgement** of a healthcare provider and personal preference and circumstances. Any further additional doses should be administered at **least 8 weeks (2 months) after the last** COVID-19 vaccine dose.	

COVID-19 Vaccine. https://www.cdc.gov/vaccines/covid-19/downloads/COVID-19-immunization-schedule-ages-6months-older.pdf

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Hepatitis A Vaccine

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Types of Hepatitis A Vaccines

- Havrix 720 EL
- Havrix 1440 EL
- Vaqta 25
- Vaqta 50

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Hepatitis A Vaccine Eligibility

Hepatitis A vaccine is recommended for the following adults:

- International travelers
- Men who have sexual contact with other men
- People who use injection or non-injection drugs
- People who have occupational risk for infection
- People who anticipate close contact with an international adoptee
- People experiencing homelessness
- People with HIV
- People with chronic liver disease

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Hepatitis A Vaccine Schedule

- Any person who is not fully vaccinated and requests vaccination (identification of risk factor not required):
  - ✓2-dose series Havrix 6–12 months apart
  - ✓2-dose series Vaqta 6–18 months apart
- Any person who is not fully vaccinated and who is at risk for hepatitis A virus infection:
  - ✓2-dose series Havrix 6–12 months apart
  - ✓2-dose series Vaqta 6–18 months apart

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Hepatitis B Vaccine

35

Types of Hepatitis B Vaccines

- Engerix-B
- Heplisav-B
- Recombivax HB

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Hepatitis B Vaccines Eligibility

- The Hepatitis B vaccine is recommended for all adults aged 19 through 59 years, and adults aged 60 years or older with risk factors for hepatitis B infection
- Adults who are 60 years or older without known risk factors for hepatitis B may also receive hepatitis B vaccine

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Hepatitis B Vaccine Eligibility

Risk factors for hepatitis B:

- Persons at risk for infection by sexual exposure
- Sex partners of persons who test positive for hepatitis B surface antigen
- Sexually active persons who are not in a long-term, mutually monogamous relationship (e.g., persons with more than one sex partner during the previous 6 months)
- Persons seeking evaluation or treatment for a sexually transmitted infection
- Men who have sex with men
- Persons at risk for infection by percutaneous or mucosal exposure to blood

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Hepatitis B Vaccine Eligibility- Continuation

- Persons with current or recent injection use
- Household contacts of persons who test positive Hepatitis B
- Residents and staff of facilities for persons with developmental disabilities
- Health care and public safety personnel
- Persons on maintenance dialysis
- Persons with diabetes at the discretion of the treating clinician

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Hepatitis B Eligibility- Continuation

- International travelers to countries with high or intermediate levels of endemic hepatitis B virus infection
- Persons with hepatitis C virus infection
- Persons with chronic liver disease
- Persons with HIV infection
- Incarcerated persons

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Hepatitis B Vaccine Schedule

- 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 are used at least 4 weeks apart
  - ✓3-dose series Engerix-B, PreHevbrio, or Recombivax HB at 0, 1, 6 months

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Hepatitis A/B Vaccine

42

Types of Hepatitis A/B Vaccine

- Twinrix

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Hepatitis A/B Eligibility

- Same recommendation and eligibility as Hepatitis A and B separated Vaccines

Schedule:

- Any person who is not fully vaccinated and who is at risk for hepatitis
  - ✓ 3-dose series HepA-HepB **(Twinrix at 0, 1, 6 months)**

44

Human Papilloma Virus (HPV) Vaccine

45

Types of HPV Vaccine

- Gardasil-9

46

HPV Vaccine Eligibility

- Is a routine Vaccine that should be administered starting at the age of 9-14 years old.
- Age ranges recommended for routine and catch-up vaccination or shared clinical decision-making also apply in special situations
  - ✓ **Immunocompromising conditions**, including HIV infection: 3-dose series, even for those who initiate vaccination at age 9 through 14 years

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HPV Vaccine Schedule

- All persons up through age 26 years: 2- or 3-dose series depending on age at initial vaccination or condition
  - ✓Age 9–14 years at initial vaccination and received 1 dose or 2]doses less than 5 months apart: 1 additional dose
  - ✓Age 9–14 years at initial vaccination and received 2 doses at least 5 months apart: HPV vaccination series complete, no additional dose needed
  - ✓Age 15 years or older at initial vaccination: 3-dose series at 0. 1–2 months, 6 months

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HPV Vaccine Schedule

Shared clinical decision-making

- ✓Adults age 27–45 years: Based on shared clinical decision-making, complete a 2-dose series

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Measles, Mumps, and Rubella (MMR) Vaccine

50

Types of MMR Vaccine

- M-M-RII

51

MMR Vaccine Eligibility

- Adults who do not have presumptive evidence of immunity should get at least one dose of MMR vaccine
- Adults who are going to be in a setting that poses a high risk for measles or mumps transmission. These adults include
  - Students at post-high school education institutions
  - Healthcare personnel
  - International travelers

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MMR Vaccine Schedule

- No evidence of immunity to measles, mumps, or rubella:
  - ✓**1 dose**
- HIV infection:
  - ✓ **2-dose series at least 4 weeks apart**
- Severe immunocompromising conditions:
  - ✓**MMR contraindicated**

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MMR Vaccine Schedule- Continuation

- Students in postsecondary educational institutions, international travelers, and household or close, personal contacts of immunocompromised persons with no evidence of immunity to MMR:
  - ✓2-dose series at least 4 weeks apart if previously did not receive any doses of MMR or 1 dose if previously received 1 dose MMR
- Health care personnel:
  - ✓2-dose series at least 4 weeks apart for protection against measles or mumps or 1 dose for protection against rubella

54

Pneumococcal Vaccine

55

Types of Pneumococcal Vaccine

- Prevnar 20 (PCV20)
- Pneumovax 23 (PPSV23)
- Vaxneuvance (PCV15)

56

Pneumococcal Vaccine Eligibility

- Adults 19 through 64 Years old who had not received the vaccine or with certain risk conditions:
  - ✓Alcoholism or cigarette smoking
  - ✓Cerebrospinal fluid leak
  - ✓Chronic heart disease
  - ✓Chronic lung disease, including chronic obstructive pulmonary disease, emphysema, and asthma
  - ✓Cochlear implant
  - ✓Decreased immune function from disease or drugs
  - ✓Diabetes mellitus
- Ages 65 years or older

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Pneumococcal Vaccine- Schedule

- For these adults who never received any pneumococcal vaccine, regardless of risk condition:
  - ✓Give 1 dose of PCV15 or PCV20
  - ✓When PCV15 is used, it should be followed by a dose of PPSV23 at least 1 year later
  - ✓When PCV20 is used, it does not need to be followed by a dose of PPSV23. Their vaccines are then complete

58

Pneumococcal Vaccine- Schedule

- For these adults who only received PPSV23, regardless of risk condition:
  - ✓Give 1 dose of PCV15 or PCV20 at least 1 year after the most recent PPSV23 vaccination
- For these adults who only received PPSV13, regardless of risk condition:
  - ✓Give 1 dose of PCV20 or PPSV23
  - ✓The PCV20 dose should be given at least 1 year after PCV13. When PCV20 is used, their vaccines are then complete
  - ✓The PPSV23 dose should be given at least 1 year after PCV for any of the other chronic health conditions

59

Pneumococcal Vaccine- Schedule

- For older adults who have an immunocompromising condition:
  - ✓Give 1 dose of PCV20 or PPSV23. Regardless of the vaccine used, their series is complete.
  - ✓The PCV20 dose should be given at least 5 years after the last pneumococcal vaccine.
  - ✓The PPSV23 dose should be given at least 5 years after the last PPSV23 dose. It should also be given at least 8 weeks after the PCV13 dose.

60

Respiratory Syncytial Virus (RSV) Vaccine

61

Types of RSV Vaccine

- Abrysvo- Pfizer
- Arexvy- GSK

62

RSV Vaccine Eligibility

- Pregnant women and adults 60 and older may receive a single dose of the RSV vaccine, using shared clinical decision-making
  - ✓Lung disease (COPD and asthma)
  - ✓Chronic cardiovascular diseases
  - ✓Diabetes mellitus
  - ✓Neurologic conditions
  - ✓Kidney disorders
  - ✓Liver disorders
  - ✓Hematologic disorders
  - ✓Immunocompromise
  - ✓Other underlying conditions that a healthcare provider determines might increase the risk for severe respiratory disease

63

RSV Vaccine Schedule

- Pregnant at 32 weeks through 36 weeks and 6 days gestation from September through January in most of the continental United States:
  - ✓1 dose RSV vaccine (Abrysvo). Administer RSV vaccine regardless of previous RSV infection
- Age 60 years or older: Based on shared clinical decision-making,
  - ✓1 dose RSV vaccine (Arexvy or Abrysvo)

64

Tetanus, Diphtheria, and Pertussis (Tdap)

65

Types of Tdap Vaccine

- Adacel
- Boostrix

66

Tdap Vaccine Eligibility

- Adults who have never received Tdap should get a dose of Tdap
- Adults should receive a booster dose of either Tdap or Td (a different vaccine that protects against tetanus and diphtheria but not pertussis) every 10 years, or after 5 years in the case of a severe or dirty wound or burn

67

Tdap Vaccine Schedule

- Previously did not receive Tdap at or after age 11 years:
  - ✓1 dose Tdap, then Td or Tdap every 10 years
- Previously did not receive primary vaccination series Tdap:
  - ✓1 dose Tdap followed by 1 dose Td or Tdap at least 4 weeks later, and a third dose of Td or Tdap 6–12 months and, Td or Tdap every 10 years thereafter

68

Tdap Vaccine Schedule

- Pregnancy: 1 dose Tdap during each pregnancy, preferably in early part of gestational weeks 27–36
- Wound management: Persons with 3 or more doses of tetanus-toxoid-containing vaccine: For clean and minor wounds, administer Tdap or Td if more than10 years since last dose of Tdap; for all other wounds, administer Tdap or Td if more than 5 years

69

Td Vaccine

- Tetanus & Diphtheria
- Td is only for children 7 years and older, adolescents, and adults.
- Td is usually given as a booster dose every 10 years, or after 5 years in the case of a severe or dirty wound or burn.

70

Varicella Vaccine

71

Types of Varicella Vaccine

- Varivax

72

Varicella Vaccine Eligibility

- Adolescents and Adults (≥ age 13 years) without evidence of immunity.

73

Varicella Vaccine Schedule

- No evidence of immunity to varicella:
  - ✓2-dose series 4–8 weeks apart if previously did not receive varicella-containing vaccine; if previously received 1 dose varicella-containing vaccine, 1 dose at least 4 weeks after first dose
- Health care personnel with no evidence of immunity to varicella:
  - ✓ 1 dose if previously received 1 dose varicella-containing vaccine; 2-dose series 4–8 weeks apart if previously did not receive any varicella-containing vaccine, regardless of whether U.S.-born before 1980.
- HIV infection: Vaccination may be considered (2 doses- 3 months apart)

74

Zoster (Shingles Vaccine)

75

Types of Zoster Vaccine

- Shingrix

76

Zoster Vaccine Eligibility

- Adults 19 years and older who have a weakened immune system
- All adults 50 years and older
- You should get Shingrix even if in the past you:
  - ✓Had shingles
  - ✓Received Zostavax
  - ✓Received varicella (chickenpox) vaccine

77

Zoster Vaccine Schedule

- Immunocompromising conditions (including persons with HIV regardless of CD4 count):
  - ✓2-dose series recombinant zoster vaccine (RZV, Shingrix) 2–6 months apart
- Age 50 years or older:
  - ✓2-dose series recombinant zoster vaccine (RZV, Shingrix) 2–6 months apart, regardless of previous herpes zoster vaccine history

78

Meningococcal Vaccine

79

Types of Meningococcal Vaccine

- Bexsero
- Menactra
- MenQuadfi
- Menveo
- Trumenba

80

Meningococcal Vaccine Eligibility

Adults should get the meningococcal vaccine if:

- First-year college student living in a residence hall
- Military recruit
- Damaged spleen or your spleen has been removed
- Terminal complement deficiency
- Microbiologist who is routinely exposed to the pathogen
- Traveling or residing in countries in which the disease is common

81

Meningococcal Vaccine Schedule

- Anatomical or functional asplenia (including sickle cell disease), HIV infection, persistent complement component deficiency, complement inhibitor
  - ✓2-dose series MenACWY (Menveo or MenQuadfi) at least 8 weeks apart and revaccinate every 5 years if risk remains
- Travel in countries with hyperendemic or epidemic meningococcal disease, or microbiologists routinely exposed to Neisseria meningitidis:
  - ✓1 dose MenACWY (Menveo or MenQuadfi) and revaccinate every 5 years if risk remains

82

Meningococcal Vaccine Schedule

- First-year college students who live in residential housing (if not previously vaccinated at age 16 years or older) or military recruits:
  - ✓1 dose MenACWY (Menveo or MenQuadfi)

83

Additional Information

84

Vaccines

- Additional information on uncommon vaccines such as Yellow fever, Rabies, Polio, Japanese encephalitis, Typhoid, and Cholera can be found in the Centers for Disease Control and Prevention (CDC).

85

Vaccines That Can Be Dispensed With Prescription

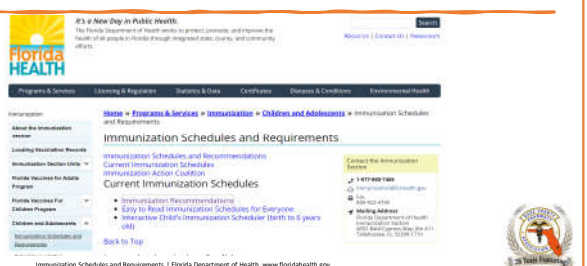
- Hepatitis A
- Hepatitis B
- Hepatitis A/B
- HPV
- MMR
- Pneumococcal
- RSV
- Tdap
- Td

86

Vaccines Updates Reliable Sources

87

Florida Health Department



Immunization Schedules and Requirements | Florida Department of Health. www.floridahealth.gov. https://www.floridahealth.gov/programs-and-services/immunization/children-and-adolescents/schedules-and-requirements/index.html

88

Florida Health Department

Immunization Schedules and Requirements | Florida Department of Health. www.floridahealth.gov. https://www.floridahealth.gov/programs-and-services/immunization/children-and-adolescents/schedules-and-requirements/index.html

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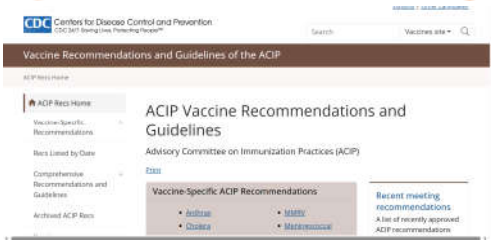
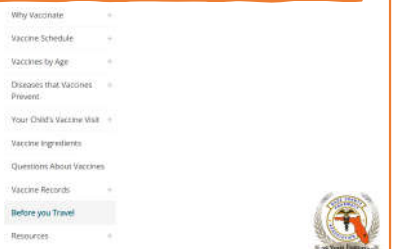
Centers for Disease Control and Prevention (CDC)



ACIP Vaccine Recommendations. Published 2019. https://www.cdc.gov/vaccines/hcp/acip-recs/index.html

90

Centers for Disease Control and Prevention (CDC)



ACIP Vaccine Recommendations. Published 2019. https://www.cdc.gov/vaccines/hcp/acip-recs/index.html

91

Questions

92

Question Number 1

True or False

The COVID-19 vaccine is considered a routine immunization schedule for all adults.

93

ANSWER: TRUE

94

Question Number 2

True or False

According to the Advisory Committee on Immunization Practices (ACIP), the use of PCV15 or PCV20 is recommended in persons who previously received PPSV23 pneumococcal vaccines.

95

ANSWER: TRUE

96

Question Number 3

True or False

CDC recommends adults 45 years and older may receive a single dose of RSV vaccine, based on discussions between the patient and health care provider.

97

ANSWER: False

Adults 60 years and older, based on comorbidities: heart or lung disease, weakened immune systems, or who live in nursing homes or long-term care facilities.

98

Thank You!

99

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- ACIP Vaccine Recommendations. Published 2019. https://www.cdc.gov/vaccines/hcp/acip-recs/index.html
- Kim DK, Riley LE, Harriman KH, Hunter P, Bridges CB. Recommended Immunization Schedule for Adults Aged 19 Years or Older, United States, 2017*. Annals of Internal Medicine. 2017;166(3):209. doi:https://doi.org/10.7326/m16-2936
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Slide 1

The Use of Monoclonal Antibodies in Ulcerative Colitis, Crohn's Disease, and Autoimmune Gastrointestinal Disorders

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Nicklaus Children's Hospital
01/21/2024

1

Slide 2

Objectives

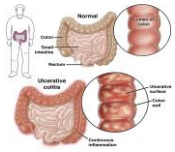
- Describe the pathophysiology of autoimmune gastrointestinal disorders
- Assess the role of monoclonal antibodies and their place in therapy for the treatment of autoimmune gastrointestinal disorders
- Compare the mechanism of action of monoclonal antibodies used for the treatment of autoimmune gastrointestinal disorders

2

Slide 3

Ulcerative Colitis (UC)

- Chronic disease affecting nearly 1 million individuals in the United States and Europe
- Inflammation can be local or widespread



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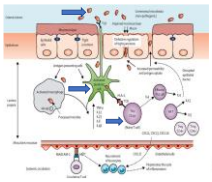
Slide 4

Pathophysiology of Ulcerative Colitis

- Dendritic cells and macrophages are exposed to lumen bacterial antigens
- Activation of CD4+ T-cells and begin an immune response
- Persistent inflammation



Slide 5

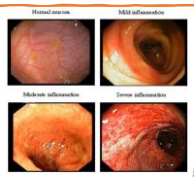
What are the symptoms of UC?

- Mild to moderate
  - Blood in stool
  - Diarrhea
  - Mild abdominal cramping
  - Urge to have a bowel movement without having to stool (tenesmus)
- Severe
  - Fever
  - Dehydration
  - Bowel incontinence
  - Weight loss
  - Anorexia

Slide 6

Diagnosis of UC

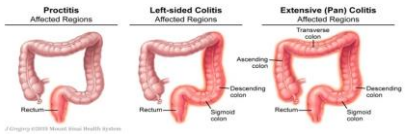
- Clinical symptoms + endoscopy & histology
- No specific test
- Diagnoses is through observation of changes over time



de Lange T. & colleagues. BMC Gastroenterol. 2004

Slide 7

Montreal Classification of Extent and Severity of UC



Kayal M, Shah S. Journal of Clinical Medicine. 2020;

Slide 8

Crohn's Disease

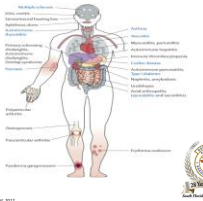
- Chronic idiopathic inflammatory bowel disease
- Estimated incidence of 3 to 20 cases per 100,000 people
- On average, the disease appears between the age of 10 to 20 years of age, then has a slight increase again at the age of 50 years

Feuerstein JD, Cheifetz AS. Mayo Clin Proc. 2017

Slide 9

Presentation of Crohn's Disease

- Initially, patients often present with nonspecific symptoms such as intermittent abdominal pain and diarrhea
- Disease progression leads to penetrating or stricturing disease

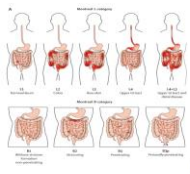


Baumgart DC, Sandborn WJ. Lancet. 2012

Slide 10

Stratification of Crohn's Disease

- Can appear on any part of the gastrointestinal tract.
- Montreal Classification is also used to help guide clinicians
- Extent of inflammation is also assessed



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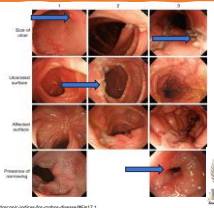
Baumgart DC, Sandborn WJ. Lancet. 2012.

Slide 11

Diagnosis of Crohn's Disease

- Symptoms + endoscopy/radiologic findings
- Thorough endoscopy is necessary to assess for surgical indications
- Ulcers and strictures are common



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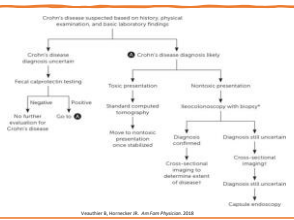
https://abdominalkey.com/endoscopic-indices-for-crohns-disease/#Fig17.1

Slide 12

Diagnosis of Crohn's Disease



12

Vreuther B, Horrocker JR. Am Fam Physician. 2018.

Slide 13

Biologic Agents Indicated for Autoimmune Gastrointestinal Disease

13

Slide 14

Tumor Necrosis Factor Blockers

Biologic agent	Molecular target	Use in disease severity category	Induction	Maintenance	Disease state		Strength of recommendation
Infliximab (Remicade)	Anti-TNF	Moderate to severe	Yes	Yes	UC	CD	Strong
Adalimumab (Humira)	Anti-TNF	Moderate to severe	Yes	Yes	UC	CD	Strong
Certolizumab (Cimzia pegol)	Anti-TNF	Moderate to severe	Yes	Yes	X	CD	Strong
Golimumab (Simponi)	Anti-TNF	Moderate to severe	Yes	Yes	UC	X	Strong

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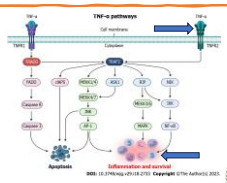
Slide 15

TNF in Autoimmune GI Disease

- Tumor necrosis factor alpha (TNF) agents
- Proinflammatory signaling
- Over-expression of TNF receptors has been correlated with disease activity



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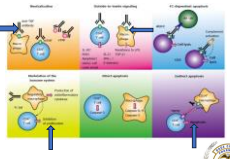
Slide 16

Proposed Mechanism of TNF Blocking Agents

- Anti-TNF agents can bind to both soluble (sTNF) and membrane bound (mTNF)
- mTNF-anti TNF complexes higher clinical efficacy than sTNF-anti TNF complexes



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Slide 17

IL-23 Blockers

Biologic agent	Molecular target	Use in disease severity category	Induction	Maintenance	Disease state		Strength of recommendation
Ustekinumab (Stelara)	IL-12 & IL-23 blocker	Moderate to severe	Yes	Yes	UC	CD	Moderate
Risankizumab (Skyrizi)	IL-23 blocker	Not included in guidelines	Yes	Yes	X	CD	N/A
Mirikizumab (Omvoh)	IL-23 blocker	Not included in guidelines	Yes	Yes	UC	X	N/A

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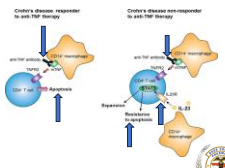
Slide 18

Non-Responders to anti-TNF Biologics

- High TNFR2 expression usually predicts response
- Non-responders present with a different phenotype
- Macrophages are activated via an alternative pathway



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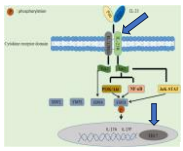
Slide 19

Mechanism of Action

- Blocking IL23 results in prevention of downstream signaling
- Decrease in proinflammatory gene expression and decreased activation of TH17 cells



Slide 20

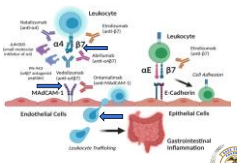
Alpha-4 & 7 Integrin Blockers

Biologic agent	Molecular target	Use in disease severity category	Induction	Maintenance	Disease state		Strength of recommendation
Natalizumab (Tysabri)	Alpha-4 integrin blocker	Conditionally recommend against use	Yes	Yes	X	CD	Conditional/Moderate
Vedolizumab (Entyvio)	Alpha-4 beta-7 integrin inhibitor	Moderate to Severe	Yes	Yes	UC	CD	Conditional/Low-moderate

Slide 21

Alpha-4 & 7 Integrin Blockers

- Infiltration of leukocytes to the GI tract
- Alpha-4 integrin is specific to the GI tract
- Inhibition results in decreased migration of leukocytes to the GI lumen



Slide 22

The Evolving Role of Biologics in the Management of Autoimmune Gastrointestinal Disease

22

Slide 23

Treatment of Ulcerative Colitis

- Resolution of acute inflammatory processes
- Resolution of attendant complications (e.g., fistulas or abscesses)
- Alleviation of systemic manifestations (e.g., arthritis)
- Maintenance of remission to prevent the need for surgical intervention

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Slide 24

Treatment Shift in Ulcerative Colitis

- 2019 American College of Gastroenterology (ACG) Clinical Guideline on Ulcerative Colitis in adults strongly recommend the use of biologic agents for induction and maintenance of remission
- Use first-line in moderate to severely active disease

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Slide 25

ACT 1 & ACT 2 Trials

Rutgeers & colleagues 2006	
Objectives	Assess the efficacy of infliximab for induction and maintenance
Methods	364 patients per study randomized to infliximab (5mg/kg or 10mg/kg) for induction and maintenance or placebo
Outcomes	Decrease in Mayo score by 3 points & 30% with a decrease in rectal bleeding
Results	Week 8: 64% vs 69% vs 29% (p<0.001) Week 54: 45.5% vs 44.3% vs 19.8% (p<0.001)
Conclusions	Infliximab demonstrates continued efficacy in moderate to severe disease

25

Rutgeerts P & colleagues. *N Engl J Med.* 2005

Slide 26

GEMINI Trial

Feagan & colleagues 2013	
Objectives	Assess the efficacy to vedolizumab for induction and maintenance
Methods	1406 patients received 300mg of vedolizumab for induction Randomized into 1:1:1 ratio to receive drug every 8 weeks, every 4 weeks, or placebo
Outcomes	Mayo score decrease of at least 3 points & 30% from baseline
Results	Week 6: 47.1% vs 25.5% (p<0.001) Week 52: 41.8% vs 44.8% vs 15.9% (p<0.001 for both groups)
Conclusions	Vedolizumab is more effective for both induction and maintenance vs placebo

26

Feagan BG & colleagues. *N Engl J Med.* 2013

Slide 27

ULTRA 1 & ULTRA 2 Trials

Sands & colleagues	
Objectives	Assess the efficacy to adalimumab for induction and maintenance
Methods	494 patients with moderate to severe disease Randomized to either receive adalimumab or placebo for both induction and maintenance
Outcomes	Total score on Mayo scale <2
Results	Week 8: 16.5% vs 9.3% (p=0.019) Week 52: 17.3% vs 8.5% (p=-.004)
Conclusions	Adalimumab is more effective than placebo to induce and maintain remission

27

Sandborn WJ & colleagues. *Gastroenterology.* 2012

Slide 28

UNIFI Trial

Sands & colleagues	
Objectives	Assess the efficacy of ustekinumab for induction/maintenance
Methods	Induction: 961 randomized to ustekinumab 130mg, 6mg/kg or placebo, all groups then received ustekinumab at week 8 Maintenance: 523 randomized to 90mg of ustekinumab every 12 vs 8 weeks vs placebo
Outcomes	Mayo score <2 to indicate remission
Results	Week 8: 15.6% vs 15.5% vs 5.3% (p=<0.001) Week 44: 38.4% vs 43.8% vs 24.0% (p=0.002 and p=<0.001)
Conclusions	Ustekinumab is more effective than placebo for induction and maintenance

28

Sands BE & colleagues. N Engl J Med. 2019

Slide 29

PURSUIT Trial

Sandborn & colleagues 2013	
Objectives	Assess the efficacy of golimumab for induction/maintenance
Methods	464 patients who had response to induction therapy randomized to golimumab 50mg or 100mg or placebo every 4 weeks through 52 weeks
Outcomes	Mayo score of <2 to indicate remission
Results	Week 54: 47% vs 49% vs 31% receiving placebo (p=0.010 and p<0.001 respectively)
Conclusions	Golimumab is more effective than placebo at inducing and maintaining remission

29

Sandborn WJ & colleagues. Gastroenterology. 2014

Slide 30

Biologic Recommendations for UC

- 2020 AGA guidelines
  - 1st tier: Infliximab, vedolizumab, adalimumab (conditionally recommended for patients with less severe disease)
  - 2nd tier: Ustekinumab (if used infliximab previously)
  - 3rd tier: Golimumab
- Use first-line in moderate to severe disease

30

Rubin DT & colleagues. Am J Gastroenterol. 2019

Feuerstein JD & colleagues. Gastroenterology. 2020

Slide 31

Treatment of Crohn's Disease

- Overall goal of medication therapy is to achieve and maintain remission & prevent surgery
- 33% of patients will require surgery within 5 years of being diagnosed
- Over their lifetime, 80% of patients will have needed surgery at some point
- Surgery is not curative

31

Feuerstein JD & colleagues. *Mayo Clin Proc.* 2017

Slide 32

Treatment Shift in Crohn's Disease

- Pre early 2000s, limited to oral options with limited effectiveness
- Now biologics are recommended first line
- Endorsed the 2019 American College of Gastroenterology Clinical Guideline and the 2021 Guidelines on the Medical Management of Moderate to Severe Fistulizing Crohn's Disease from the American Gastroenterology Association (AGA)

32

Feuerstein JD & colleagues. *Gastroenterology.* 2021.
Lichtenstein GR & colleagues. *Am J Gastroenterol.* 2018

Slide 33

ACCENT I Trial

Hanauer & colleagues 2002	
Objective	Evaluate the effectiveness of infliximab vs placebo for induction and maintenance of remission
Methods	573 patients randomized to 5mg/kg vs 10mg/kg vs placebo
Outcomes	Patients in remission at week 30 as defined with CDAI <150
Results	Week 30: 39% vs 45% vs 21% (p<0.004 for both comparisons)
Conclusion	Infliximab is a viable option for Crohn's disease to induce and maintain remission where other therapies have previously failed

33

Hanauer SB, & colleagues. *Lancet.* 2002

Slide 34

CLASSIC I Trial

Hanauer & colleagues 2006	
Objectives	Evaluate the effectiveness of adalimumab vs placebo for induction of remission
Methods	299 patients received an initial dose of adalimumab then were randomized to placebo or repeat infusion at ½ dose on week 2
Outcomes	Remission at week 4 as defined by a CDAI score of <150
Results	Remission at week 4 adalimumab 40mg/20mg, 80mg/40mg, 160mg/80mg vs placebo 18% (p=0.36), 24% (p=0.06), 36% (p=0.001), 12%
Conclusion	Adalimumab is an alternative agent for induction of remission in moderate to severe Crohn's disease

34

Hanauer SB & colleagues. *Gastroenterology* 2006

Slide 35

CHARM Trial

Colombel & colleagues 2007	
Objectives	Assess the long-term use of adalimumab for maintenance of remission
Outcomes	Percentage of patients in clinical remission as defined by CDAI <150 at weeks 26 and 56
Methods	All patients received adalimumab for induction therapy, then were randomized to either adalimumab every week or every other week or placebo
Results	Week 26: In remission (40%, 47%, 17%, p<0.001) Week 56: In remission (36%, 51%, 12%, p<0.001)
Conclusions	Adalimumab is effective for maintaining remission with no significant difference between dosing strategies

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Colombel JF & colleagues. *Gastroenterology* 2007

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UNITI-1/UNITI-2 & IM-UNITI Trials

Feagan & colleagues 2016	
Objectives	Examine the efficacy of ustekinumab in primary non-responders to anti-TNF agents
Methods	Single dose induction therapy (130mg vs 6mg/kg vs placebo) Responders at week 8 then randomized to either ustekinumab every 8 or 12 weeks or placebo through 40 weeks
Outcomes	Response at week 6 (decrease in CDAI >100 points) Remission at week 44 (CDAI <150)
Results	Week 6: 51.7%, 55.5%, 28.7% (p<0.001) Week 44: 53.1%, 48.8%, 35.9% (p=0.005 & p=0.04)
Conclusions	Ustekinumab induces and maintains remission in patients non-responsive to other biologic therapy

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Feagan BG & colleagues. *N Engl J Med.* 2016

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Head-to-Head Comparison of First Line Agents?

Osterman & colleagues 2013	
Objectives	Assess the effectiveness of infliximab or adalimumab as 1st line agent
Methods	Retrospective cohort study of 1459 users of infliximab and 871 users of adalimumab
Outcomes	Continuation on therapy at week 26, surgery or hospitalization per 100 person-years
Results	Remained on 1st line agent: 49% vs 47% (OR 0.98, 95%CI 0.81-1.19) Surgery: 5.5 vs 6.9 (HR 0.79, 95%CI 0.60-1.05) Hospitalization: 11.8 vs 15.4 (HR 0.88, 95%CI 0.72-1.07)
Conclusions	Infliximab or adalimumab have similar outcomes regarding continuation and complications

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Osterman MT & colleagues. Clin Gastroenterol Hepatol. 2014

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SWITCH trial

Van Assche & colleagues 2012	
Objectives	Assess if switching between infliximab to adalimumab results in maintenance of efficacy
Methods	73 patients enrolled open-label trial, randomized to either continue infliximab or switch to subcutaneous adalimumab for 1 year
Outcomes	Need for dose optimization or interruption of treatment for loss of tolerance
Results	Dose optimization/loss of tolerance: 17/36 (47%) in the adalimumab and 6/37 (16%) in the infliximab group, (p = 0.006)
Conclusions	Elective switching from the first line agent without clinical need is associated with loss of tolerance/efficacy

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Van Assche & colleagues. Gut. 2012

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Role of Certolizumab?

Sandborn & colleagues 2007	
Objective	Assess the efficacy of certolizumab in moderate to severe disease
Methods	662 adults randomized to either 400mg of certolizumab or placebo at 0, 2, and 4 weeks then every 4 weeks for 26 weeks
Outcomes	Decrease of >100 CDAI score at week 6 and remission at week 26
Results	Week 6: 35% vs 27% (p=0.02) Week 26: 14% vs 10% (p=0.07)
Conclusion	Certolizumab shows modest improvement in CDAI score, but does not statistically improve remission rates over placebo

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Sandborn & colleagues. N Engl J Med. 2007

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Is There an Order of Biologic Reccomendations?

- 2018 AGA recommendations
- 1st tier: Infliximab, adalimumab, ustekinumab
- 2nd tier: Vedolizumab
- 3rd tier: Certolizumab pegol
- Conditionally recommended: Natalizumab

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Feuerstein & colleagues. Gastroenterology 2021

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Why not Natalizumab?

- Post marketing data shows possibility for development of PML
- Availability of other biologics that do not have similar risk
- Potential option for refractory patients
- Screen for John Cunningham virus antibody

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Knowledge Check

- Which of the following medications is FDA approved for the treatment of UC/CD in patients who are refractory to other medications and/or corticosteroid dependent?
  - A. Adalimumab (Humira)
  - B. Infliximab (Remicade)
  - C. Vedolizumab (Entyvio)
  - D. Certolizumab pegol (Cimzia)
- All of the above

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Biologics Not Included in Current Guidelines

- Risankizumab (Skyrizi) approved by the FDA for Crohn's Disease in 2022
- Mirikizumab (Omvoh) approved by the FDA for Ulcerative Colitis in 2023
- Likely will see recommendations when new guidelines are published

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Fortify Trial

Ferrante & colleagues	
Objective	Assess efficacy of risankizumab as maintenance therapy in CD
Methods	712 patients randomized to risankizumab 180mg vs 360mg vs placebo every 8 weeks
Outcomes	CDAI indicating remission
Results	Week 52: 55% vs 52% vs 40% (p=0.03 vs p=0.05)
Conclusions	Risankizumab is efficacious for maintenance of remission following successful induction therapy

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Lucent-1 & 2 Trials

D'Haens & colleagues	
Objective	Assess the efficacy of mirikizumab for induction and maintenance in UC
Methods	544 patients randomized to mirikizumab 300mg vs placebo every 4 weeks for 12 weeks, then mirikizumab 200mg or placebo every 4 weeks
Outcomes	Clinical remission at week 12 and week 40 (52 weeks overall) by Mayo score
Results	Week 12: 24.2% vs 13.3% (p<0.001) Week 40: 49.9% vs 25.1% (p<0.001)
Conclusions	Mirikizumab is more effective than placebo in inducing and maintaining clinical remssion

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Synergism with Non-Biologic Therapy

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Non-Biologic Therapies

Medication	Guideline recommendation	Induction	Maintenance	Dosing
Budesonide	Mildly active disease or part of a combination for extensive disease	Yes	Yes	9mg once daily
Cyclosporine	Conditionally for acute symptoms refractory to corticosteroids	Yes	No	2.3 to 3mg/kg every 12 hours
Methylprednisolone	Disease flares, not recommended for long term use	Yes	No	40-60mg/day
Mesalamine	Mild to moderate disease	Yes	Yes	Depends on product and formulation
AZA/Mercaptopurine	Moderate to severe disease	Yes	Yes	Initial 50mg/day Max 2.5mg/kg/day
Methotrexate	Conditionally	Yes	Yes	15mg/week
Tofacitinib	Conditionally	Yes	Yes	Induction: 22mg once daily Maintenance: 11mg once daily

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Can Biologic Agents be Used in Conjunction with Other Non-Biologic Immunomodulatory Therapies?

- Yes!
- ACG guidelines recommend using a combination of biologics with thiopurines (azathioprine, 6-mercaptopurine) to maintain disease remission over non-biologic monotherapy
- Oral corticosteroids are effective for short term use in alleviating flares

Rubin & colleagues. *Am J Gastroenterol.* 2019
Lichtenstein & colleagues. *Am J Gastroenterol.* 2018

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Knowledge Check

- Monoclonal antibodies cannot be used in conjunction with other non-biologic immunomodulatory therapies. True or False?
  - True
  - False
- FALSE

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Practical Considerations

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Anti-TNF Agents

Biologic agent	Route	Dose	Maintenance interval	Ulcerative colitis	Crohn's Disease
Infliximab (Remicade)	IV	Induction: 5mg/kg Maintenance 5-10mg/kg	8 weeks	Yes	Yes
Adalimumab (Humira)	SQ	Induction: 160mg then 80mg in 2 weeks Maintenance: 40mg	Every other week	Yes	Yes
Certolizumab (Cimzia pegol)	SQ	Induction: 400mg, repeat dose at 2 then 4 weeks after 1st Maintenance: 400mg	4 weeks	No	Yes
Golimumab (Simponi)	SQ	Induction: 200mg at 0, then 100mg at 2 weeks Maintenance: 100mg	4 weeks	Yes	No

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Anti -IL23 Agents

Biologic agent	Route	Dose	Maintenance interval	Ulcerative colitis	Crohn's Disease
Ustekinumab (Stelara)	IV/SQ	Induction: Weight based (IV) Maintenance: 90mg SQ	8 weeks	Yes	Yes
Risankizumab (Skyrizi)	IV/SQ	Induction: 600mg at 0, 4, and 8 weeks Maintenance: 180-360mg	180mg at week 12 then 360mg every 8 weeks	No	Yes
Mirikizumab (Omvoh)	IV/SQ	Induction: 300mg at 0,4, and 8 weeks Maintenance: 200mg	Starting week 12 then every 4 weeks thereafter	Yes	No

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Anti -Integrin Agents

Biologic agent	Route	Dose	Maintenance interval	Ulcerative colitis	Crohn's Disease
Natalizumab (Tysabri)	IV	Induction: 300mg Maintenance: 300mg	4 weeks	No	Yes
Vedolizumab	IV/SQ	Induction & maintenance IV: 300mg at 0,2, and 6 weeks SQ: 108mg after at least 2 IV doses	8 weeks for IV 2 weeks for SQ	No	Yes

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Monitoring Considerations

Biologic agent	Special considerations/monitoring
Infliximab (Remicade)	HBV/TB screen prior to starting CBC and LFT at baseline and at least every 6 to 12 months, avoid live vaccine due to risk of vaccine associated infection
Adalimumab (Humira)	HBV/TB screen prior to starting CBC and LFT at baseline and periodically during treatment, avoid live vaccine due to risk of vaccine associated infection
Certolizumab (Cimzia-pegol)	Hepatitis/TB screen prior to starting CBC, CMP at baseline and periodically, avoid live vaccine administration during therapy due to risk of vaccine associated infection
Golimumab (Simponi)	HBV/TB screen prior to starting CBC, LFT at baseline and periodically, avoid live vaccine administration during therapy due to risk of vaccine associated infection
Natalizumab (Tysabri)	LFT at baseline, Increased risk of PML, avoid live vaccine administration during therapy due to risk of vaccine associated infection
Ustekinumab (Stelara)	HBV/HCV/TB screen prior to starting CBC at baseline and periodically, avoid live vaccine administration during therapy due to risk of vaccine associated infection
Vedolizumab (Entyvio)	TB screen prior to starting LFTs periodically Patients wanting to transition to SQ must receive at least 2 IV infusions, avoid live vaccine administration during therapy due to risk of vaccine associated infection
Risankizumab (Skyrizi)	HBC/HCV/TB screen prior to starting CBC, CMP, LFT at baseline and periodically, avoid live vaccine administration during therapy due to risk of vaccine associated infection
Mirikizumab (Omvoh)	TB screen prior to starting LFT at baseline and periodically, avoid live vaccine administration during therapy due to risk of vaccine associated infection

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Infusion Reaction Management

- Biologics infused over IV route
- Occur with the first dose or subsequent doses
- Slowing infusion rate or addition of antipyretics/antihistamines/corticosteroid prior to infusion and as needed throughout

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Knowledge Check

- Golimumab is the only TNF-a inhibitor that may be used with the MMR vaccine. True or False?
- FALSE

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Biologics for Non-IBD

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Celiac Disease

- In progress clinical trial of PRV-015
- Phase 2 trial, randomized double blind
- Primary outcome: Celiac Disease Patient-Reported Outcome at 23 weeks
- Secondary outcomes: Safety and immunogenicity
- Study completes 2024

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Thank you

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South Florida Pharmacy Residents

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Questions?

South Florida Pharmacy Residents

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You Can't Spell Healthcare Without THC: Updates in Medical Marijuana

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January 21, 2024

1

Objectives

Review the FDA approved cannabis products

Discuss qualifying medical conditions

Review scheduling of cannabis products

2

Table of Contents

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Abbreviations

- Tetrahydrocannabinol (THC)
- Cannabidiol (CBD)
- Food and Drug Administration (FDA)
- Medical Marijuana Treatment Centers (MMTC)
- Department of Health and Human Services (HHS)
- Controlled Substances Act (CSA)

4

Difference Between Cannabis and Marijuana

- Cannabis
  - All products derived from the plant *Cannabis sativa*
  - The cannabis plant contains about 540 chemical substances
- Tetrahydrocannabinol (THC)
  - The substance primarily responsible for the effects on a person's mental state
- Marijuana
  - Parts of or products from the plant *Cannabis sativa* that contain substantial amounts of THC
- Some cannabis plants contain very little THC
  - Under U.S. law, these plants are considered "industrial hemp" rather than marijuana

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Cannabis

- Cannabinoids
  - Naturally occurring compounds found in the plant *Cannabis sativa L.*
  - There are over 80 different cannabinoids
- Two well-known cannabinoids:
  - Tetrahydrocannabinol (THC)
  - Cannabidiol (CBD)
- Plants are grown to produce varying concentrations of cannabinoids – THC or CBD
- These plant variations are called cultivars

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Cannabis-Derived Compounds

- Compounds occurring naturally in the plant – like CBD and THC
- Extracted directly from the plant
- Can be used to manufacture drug products
- Example:
  - Highly-purified CBD extracted from the plant

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Cannabis-Related Compounds

- Synthetic compounds created in a laboratory
  - Nabilone
- Can be used to manufacture drug products
- Some synthetic compounds may also occur naturally in the plant
  - Dronabinol

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Medical Marijuana

- Marijuana for medical use by a qualified patient to treat qualifying medical conditions
  - "Medical use" means the acquisition, possession, use, delivery, transfer, or administration of marijuana authorized by a physician certification

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Qualified Patient

- Resident of this state
- Has been added to the medical marijuana use registry by a qualified physician to receive marijuana or a marijuana delivery device for a medical use
- Has a qualified patient identification card

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Qualifying Conditions

- A patient must be diagnosed with at least one of the following conditions to qualify to receive marijuana or a marijuana delivery device:

- Cancer
- Epilepsy
- Glaucoma
- Positive status for human immunodeficiency virus
- Acquired immune deficiency syndrome
- Posttraumatic stress disorder
- Amyotrophic lateral sclerosis
- Crohn's disease
- Parkinson's disease
- Multiple sclerosis
- A terminal condition diagnosed by a physician other than the qualified physician issuing the physician certification
- Chronic nonmalignant pain

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Unauthorized Medical Marijuana Use

- Marijuana that was not purchased or acquired from a medical marijuana treatment center
- Marijuana in the form of commercially produced food items other than edibles or of marijuana seeds
- Use or administration of any form or amount of marijuana in a manner that is inconsistent with the qualified physician's directions or physician certification
- Transfer of marijuana to a person other than the qualified patient for whom it was authorized
- Use or administration of marijuana in the following locations:
  - In any public place, public transportation, school bus, a vehicle, an aircraft, or a motorboat
    - Except for low-THC cannabis not in a form for smoking
  - Place of employment, except when permitted by his or her employer
  - In a state correctional institution
  - On school grounds
  - The smoking of marijuana in an enclosed indoor workplace

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Question #1:

True or false: There are currently no cannabis-derived or synthetic cannabis-related drug products approved by the FDA

- True
- False

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Question #1:

True or false: There are currently no cannabis-derived or synthetic cannabis-related drug products approved by the FDA

- True
- **False**

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FDA Approved Products

- To date, the FDA has not approved a marketing application for cannabis for the treatment of any disease or condition

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FDA Approved Products

- One cannabis-derived drug product
  - Epidiolex (cannabidiol)
- Three synthetic cannabis-related drug products:
  - Marinol (dronabinol)
  - Syndros (dronabinol)
  - Cesamet (nabilone)
- Only available with a prescription from a licensed healthcare provider
  - Epidiolex is a schedule V
  - Marinol, Syndros, Cesamet are schedule III

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Epidiolex (cannabidiol)

- Contains a purified form of the drug substance CBD
- FDA approved for the treatment of:
  - Seizures associated with Lennox-Gastaut syndrome or Dravet syndrome in patients 2 years of age and older

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Marinol, Syndros (dronabinol)

- Active ingredient dronabinol
  - Synthetic delta-9- THC
  - Considered the psychoactive intoxicating component of cannabis
  - Responsible for the "high" people may experience from using cannabis
- FDA approved for:
  - Nausea associated with cancer chemotherapy and for the treatment of anorexia associated with weight loss in AIDS patients

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Cesamet (nabilone)

- Active ingredient nabilone
  - Has a similar chemical structure to THC
  - Synthetically derived
- FDA approved indication for nausea associated with cancer chemotherapy

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Question #2:

Which of the following is NOT an FDA approved indication for the use of cannabis derived or cannabis-related drug products?

a. Seizures associated with Lennox-Gastaut or Dravet syndrome
b. Nausea associated with cancer chemotherapy
c. Anorexia associated with weight loss in AIDS patients
d. Panic attacks associated with post-traumatic stress disorder

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Question #2:

Which of the following is NOT an FDA approved indication for the use of cannabis derived or cannabis-related drug products?

a. Seizures associated with Lennox-Gastaut or Dravet syndrome
b. Nausea associated with cancer chemotherapy
c. Anorexia associated with weight loss in AIDS patients
d. Panic attacks associated with post-traumatic stress disorder

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Panic Attacks

A Case of Panic Attacks Developing After 10 Years of Chronic Cannabis Use in a Patient With No Prior Psychiatric History

Grace A. Johnson [1], Lucy Guerra [1], Asa Oxner [2]

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MOOD AND ANXIETY DISORDERS: EDITED BY SIDNEY H. KENNEDY AND HANS-ULRICH WITTCHEN

The role of cannabis in treating anxiety an update

Van Ameringen, Michael[A,B]; Zhang, Jasmine[B]; Patterson, Beth[A,B]; Turna, Jasmine[B,C,D]

Author Information

Current Opinion in Psychiatry 33(1):p 1-7, January 2020. | **DOI:** 10.1097/YCO.0000000000000566

Lifetime associations between cannabis, use, abuse, and dependence and panic attacks in a representative sample

Michael J. Zvolensky [a], Amit Bernstein [a], Natalie Sachs-Ericsson [b], Norman B. Schmidt [b], Julio D. Buckner [b], Marcel O. Bonn-Miller [a]

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Registered Physicians

- From January 6, 2023 to December 8, 2023 the number of registered physicians has increased from 2,638 to 2,740

medical-marijuana-scaled.jpg (2560×1709) (lifecanmmd.com)

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Qualified Physicians

- Before being approved as a qualified physician and before each license renewal, a physician must:
  - Successfully complete a 2-hour course and subsequent examination offered by the Florida Medical Association or the Florida Osteopathic Medical Association
    - The course and examination must be administered at least annually and may be offered in a distance learning format, including an electronic, online format that is available upon request
- A qualified physician may not be employed by, or have any direct or indirect economic interest in, a medical marijuana treatment center or marijuana testing laboratory

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Steps to Issue a Physician Certification

1. Conduct an examination and a full medical history assessment of the patient
   - For initial certification to a patient, the qualified physician must conduct an in-person physical examination of the patient
   - For certification renewals, a qualified physician who has issued a certification to a patient after conducting an in-person physical examination may conduct subsequent examinations of that patient through telehealth
2. Diagnose the patient with at least one qualifying medical condition
3. Determine and document in the patient's medical record that the medical use of marijuana would likely outweigh the potential health risks for the patient
   - Patient <18 years of age, a second physician must concur with this determination

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Steps to Issue a Physician Certification

4. Review the patient's controlled drug prescription history in the prescription drug monitoring program database
5. Review the medical marijuana use registry and confirmed that the patient does not have an active physician certification from another qualified physician

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Steps to Issue a Physician Certification

6. Electronically register as the issuer of the physician certification for the named qualified patient on the medical marijuana use registry
   a. Enter into the registry the contents of the physician certification
      - Patient's qualifying condition
      - Dosage not to exceed the daily dose amount determined by the department
      - The amount and forms of marijuana authorized for the patient
      - Any types of marijuana delivery devices needed by the patient for the medical use of marijuana
   b. Update the registry within 7 days after any change is made to the original physician certification to reflect such change
   c. Deactivate the registration of the qualified patient and the patient's caregiver when the physician no longer recommends the medical use of marijuana for the patient

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Steps to Issue a Physician Certification

7. Obtains the voluntary and informed, written consent of the patient for medical use of marijuana each time the qualified physician issues a physician certification for the patient
   - The patient, or the patient's parent or legal guardian if the patient is a minor, must sign the informed consent acknowledging that the qualified physician has sufficiently explained its content
   - Maintain the signed informed consent in the patient's medical record
   - A standardized informed-consent form adopted by the Board of Medicine and the Board of Osteopathic Medicine must be used

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Informed Consent Requirements

- The Federal Government's classification of marijuana as a Schedule I controlled substance
- The approval and oversight status of marijuana by the FDA
- The current state of research on the efficacy of marijuana to treat the qualifying conditions
- The potential for addiction
- The potential effect that marijuana may have on a patient's coordination, motor skills, and cognition, including a warning against operating heavy machinery, operating a motor vehicle, or engaging in activities that require a person to be alert or respond quickly

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Informed Consent Requirements

- The potential side effects of marijuana use, including the negative health risks associated with smoking marijuana
- The risks, benefits, and drug interactions of marijuana
- That the patient's deidentified health information contained in the physician certification and medical marijuana use registry may be used for research purposes

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Increase in Number of Registered Patients

- From January 6, 2023 to December 8, 2023 the number of registered medical marijuana cards has increased from 781,354 to 862,824

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Types of Products

- Flower/Bud
- Edibles
- Concentrates
- Hash
- Low-THC cannabis

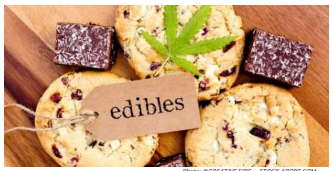

Photo: ©CREATIVE FIRE – STOCK.ADOBE.COM

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Medical Marijuana Treatment Centers

After initial licensure, each MMTC must receive authorization at three stages prior to dispensing low-THC cannabis or medical marijuana:

- Cultivation authorization
- Processing authorization
- Dispensing authorization

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MMTC Dispensations for December 30, 2022 – January 5, 2023:

MMTC Name	Dispensing Locations	Medical Marijuana (mgs THC)	Low-THC Cannabis (mgs CBD)	Marijuana in a Form for Smoking (oz)
Trulieve	123	90,980,970	1,123,722	40,087.289
MÜV	62	32,859,118	128,425	9,587.799
Ayr Cannabis Dispensary	56	39,144,418	0	7,695.657
Curaleaf	55	39,573,574	234,300	12,365.000
Surterra Wellness	45	21,909,513	1,215,963	5,075.824
Fluent	29	13,315,345	62,960	3,582.416
VidaCann	26	5,792,306	68,009	1,306.381
Sunnyside*	21	3,320,919	47,023	1,500.765
GrowHealthy	18	4,824,150	11,185	3,062.883
Green Dragon	18	1,725,359	2,048	191.393
Sanctuary Cannabis	16	3,095,245	26,613	2,047.370
Cannabist	14	4,620,769	0	1,841.471
Sunburn	8	972,411	0	807.472
GTI (Rise Dispensaries)	7	1,044,752	7,365	1,013.219
Insa – Cannabis for Real Life	5	353,208	0	297.729
HT Medical Cannabis	3	744,036	0	218.498
Jungle Boys	3	839,005	0	1,207.101
The Flowery	2	3,088,467	0	833.727
Cookies Florida, Inc.	1	175,181	0	242.457
Planet 13 Florida, Inc.	0	0	0	0
Revolution Florida	0	0	0	0
Gold Leaf	0	0	0	131.696
Total	512*	268,372,746	2,927,613	93,096.041

MMTC Dispensations for December 1 – 7, 2023:

MMTC Name	Dispensing Locations	Medical Marijuana (mgs THC)	Low-THC Cannabis (mgs CBD)	Marijuana in a Form for Smoking (oz)
Trulieve	129	97,002,915	515,755	42,719.898
MÜV	73	30,627,842	202,106	10,824.697
Ayr Cannabis Dispensary	63	38,341,367	239,885	4,905.126
Curaleaf	61	34,163,911	160,000	9,636.732
Surterra Wellness	45	29,948,124	1,215,229	7,490.392
Green Dragon	36	4,000,491	721	1,277.981
FLUENT	33	12,306,919	69,100	4,455.942
Sunnyside*	33	8,139,710	122,653	4,264.178
VidaCann	26	5,183,819	83,739	2,305.194
Sanctuary Cannabis	21	4,100,099	69,925	2,618.371
GrowHealthy	18	7,819,596	2,110	3,471.928
Cannabist	14	3,819,927	35,628	1,395.214
GTI (Rise Dispensaries)	14	3,400,484	15,178	1,777.495
Sunburn	11	7,690,168	0	2,308.471
Insa – Cannabis for Real Life	9	1,920,556	0	759.916
Jungle Boys	8	2,502,102	0	2,891.374
The Flowery	7	4,795,347	0	2,113.681
House of Platinum Cannabis	4	219,771	0	299.230
Cookies Florida, Inc.	4	791,520	0	371.412
Gold Leaf	1	500,870	0	87.111
Planet 13 Florida, Inc.	0	0	0	0
Revolution Florida	0	0	0	0
Prosperity Medical, LLC	n/a	0	0	0
Terry Dorrell Gwinn	n/a	0	0	0
Total	610*	295,934,878	2,726,019	105,837.064

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Question#3:

Marijuana is classified as a schedule I drug, what defines a schedule I drug?

a. Drugs with no currently accepted medical use and a high potential for abuse

b. Drugs that are can easily be forged for illegal sales

c. Any substance that produces a state of euphoria

d. Patients must be registered with their state government in order to legally use the drug in this schedule class

36

Question#3:

Marijuana is classified as a schedule I drug, what defines a schedule I drug?

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b. Drugs that are can easily be forged for illegal sales

c. Any substance that produces a state of euphoria

d. Patients must be registered with their state government in order to legally use the drug in this schedule class

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Question #3 Explanation

- Answer: A.
- Although the FDA approved indications for cannabis derived drug products, marijuana is still classified at CI.
- Patients with medical marijuana do register with the state to use it, however scheduling has not been updated as of yet

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Legend Drugs

- A legend drug (or prescription medication) is a drug, chemical, or substance that:
  - Has been approved by the FDA
  - Requires a prescription from a licensed medical practitioner
- Receive the name “legend drug” because specific symbols or information are required to be printed on the label
  - Known as a legend
- Rx symbol must appear on the legend to communicate that a pharmacist is authorized to fill the prescription by a licensed med practitioner when the substance is prescribed for human use

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Drug Schedules

- Drugs, substances, and certain chemicals used to make drugs are classified into five schedules depending upon
  - Acceptable medical use
  - Abuse or dependency potential
- The abuse rate is a determinate factor in the scheduling of the drug

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Schedule I

- Drugs, substances, or chemicals with no currently accepted medical use and a high potential for abuse
- Schedule I drugs are:
  - Heroin
  - Lysergic acid diethylamide (LSD)
  - Marijuana (cannabis)
  - 3,4-methylenedioxymethamphetamine (ecstasy)
  - Methaqualone
  - Peyote

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Schedule II

- Drugs, substances, or chemicals with a high potential for abuse, with use potentially leading to severe psychological or physical dependence
- Considered dangerous
- Schedule II examples:
  - Cocaine*
  - Amphetamine salts
  - Methadone
  - Hydromorphone
  - Oxycodone
  - Fentanyl

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Schedule III

- Drugs, substances, or chemicals with a moderate to low potential for physical and psychological dependence
- Schedule III drugs are:
  - Products containing less than 90 milligrams of codeine per dosage unit (acetaminophen with codeine)
  - Ketamine
  - Anabolic steroids
  - Testosterone

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Schedule IV

- Drugs, substances, or chemicals with a low potential for abuse and low risk of dependence
- Schedule IV drug examples:
  - Alprazolam
  - Diazepam
  - Lorazepam
  - Zolpidem
  - Tramadol

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Schedule V

- Drugs, substances, or chemicals with lower potential for abuse than schedule IV and consist of preparations containing limited quantities of certain narcotics
- Generally used for antidiarrheal, antitussive, and analgesic purposes
- Schedule V drug examples:
  - Cough preparations with <200 mg of codeine /100 milliliters (Guaifenesin AC)
  - Diphenoxylate and atropine
  - Pregabalin

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Current Cannabis Schedule

Cannabis is currently listed as a Schedule I controlled substance under the CSA

Schedule I substances are defined as drugs with no currently accepted medical use and a high potential for abuse

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Proposed Change in Scheduling

- In August 2023 the HHS (Department of Health and Human Services) issued a recommendation to the DEA that marijuana be classified from schedule I to schedule III

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Next Steps

1. DEA will consider marijuana reclassification under three criteria:
   - Potential for abuse
   - Potential for medical use
   - Extent of safety and addiction concerns
2. DEA will submit their own recommendation as a proposal to the attorney general
3. The attorney general will make the final ruling

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- What rescheduling to Schedule III would mean for the cannabis industry ... (n.d.). https://www.reuters.com/legal/litigation/what-rescheduling-schedule-iii-would-mean-cannabis-industry-2023-09-12/
- ➡ *difference between legend drugs and controlled substances*. Differences Finder. (2023, March 21). https://differencesfinder.com/difference-between-legend-drugs-and-controlled-substances/

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Thank You!

- Questions?

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Don't Forget These – Updates in Alzheimer's Treatments

Juhi Saxena, PharmD, M.S.
PGY-1 Pharmacy Resident
Mount Sinai Medical Center
Sunday, January 21, 2024

28 Years Featuring
South Florida Pharmacy Residents

1

Objectives

1. Provide an overview of Alzheimer's disease state
2. Discuss current treatment guidelines for the management of Alzheimer's disease
3. Identify new FDA approved treatment for Alzheimer's disease

2

Abbreviations

AD	Alzheimer's Disease
Aβ	Amyloid Beta
PET	Positron Emission Tomography
MMSE	Mini-Mental State Examination
AChE	Acetylcholinesterase
CMAI	Cohen-Mansfield Agitation Inventory
MOA	Mechanism of Action
ODT	Orally Disintegrating Tablet
QHS	Every Night at Bedtime
BID	Twice a Day
ER	Extended Release

CDR	Clinical Dementia Rating Scale
SOB	Sum of Boxes

3

Background

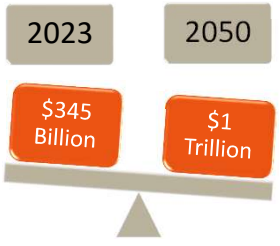
4

Epidemiology

- 6 million Americans are living with Alzheimer's
- 1/3 seniors dies with Alzheimer's or another dementia
- Incidence nearly doubles for every 5 years after 65
- Lifetime risk at age 45: 1/5 for women & 1/10 for men

5

Economic Costs – United States



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Projections – United States

In 2030, there could be 70 million people aged over 65, and by 2050, this number may increase to 82 million

16 million individuals may have AD by 2050

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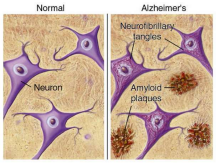
Pathophysiology[1]

- Anatomical structures
  - Neuritic (amyloid) plaque concentrations increased in the hippocampus, amygdala, and cerebral cortex
  - Presence of neurofibrillary tangles (consisting of abnormally phosphorylated tau protein) can disrupt cellular function and lead to cellular degeneration and death
  - Chronic depression has been associated with an increase in neurofibrillary tangles and amyloid plaque in the hippocampus



https://www.brightfocus.org/news/amyloid-plaques-and-neurofibrillary-tangles

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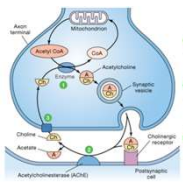
Pathophysiology (cont'd)

- Neurotransmitters
  - Loss of choline acetyltransferase and AChE activity and degeneration of cholinergic neurons
  - In moderate to severe AD, excessive glutamate is released, causing calcium influx into neurons and speeding up cell death



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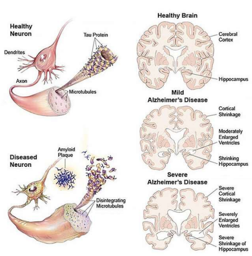
Clinical Course

- Gradual onset and slowly progressive
- Episodic memory, executive function, visuospatial function, and word-finding difficulties are affected earlier
- Motor, behavioral, and sensory functioning occur later
- During final stages patients are dependent on others for care
- Death occurs in approximately 8-10 years after diagnosis

10

Stages



Early
Symptoms are mild and characterized by general forgetfulness

Middle
Symptoms are more disabling and additional care may be needed

Late
Symptoms are significant and apparent

https://www.brightfocus.org/alzheimers-disease/infographic/progression-alzheimers-disease

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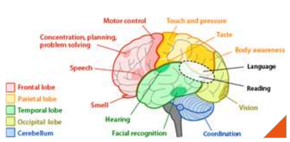
Severity



Mild Cognitive Impairment
Duration: 7 years
Disease begins in medial temporal lobe

Mild Alzheimer's
Duration: 2 years
Disease spreads to lateral temporal & parietal lobes

Moderate Alzheimer's
Duration: 2 years
Disease spreads to frontal lobe

Severe Alzheimer's
Duration: 3 years
Disease spreads to occipital lobe

https://askabiologist.asu.edu/brain-regions

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Known or Suspected Causes[1]

Early Onset (before 65)

- Increasing age, genetics, down syndrome, head trauma, depression, lower education level

Late Onset (65 and older)

- Family history, cardiovascular risk factors

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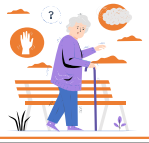
Signs & Symptoms[1]

Subjective

- Loss of function from cognitive domains (e.g. comprehension, application)
- In the final stages: develop gait abnormalities, motor disturbances, lose communication abilities and become dependent on others for total care



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Signs & Symptoms (cont'd)

Objective

- Aβ peptide: build up in the brain and eyes, which are identified by PET tracers
- Tau protein: raised levels found in patients with AD
- Three to four-point annual loss on the MMSE
- Genetic testing of various genetic markers have been investigated, specifically in early-onset AD, though there is no clinical application for it at this time

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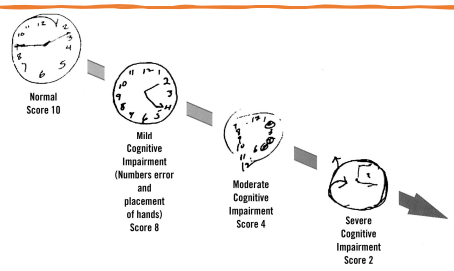
Signs & Symptoms (cont'd)



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Aging or Alzheimer's?

Signs of Alzheimer's	Typical Age-Related Changes
Poor judgment and decision making	Making a bad decision occasionally
Inability to manage a budget	Missing a monthly payment
Losing track of the date or the season	Forgetting which day it is and remembering later
Difficulty having a conversation	Sometimes forgetting which word to use
Misplacing things and being unable to retrace steps to find them	Losing things from time to time

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Pop Quiz #1

Which neurotransmitter is most prominently affected in the early stages of Alzheimer's disease, leading to cognitive and memory deficits?

a. Dopamine
b. Serotonin
c. Acetylcholine
d. Glutamate

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Pop Quiz #1

Which neurotransmitter is most prominently affected in the early stages of Alzheimer's disease, leading to cognitive and memory deficits?

a. Dopamine (Schizophrenia, Bipolar disorder, MDD, ADHD, Parkinson's)
b. Serotonin (MDD)
c. Acetylcholine
d. Glutamate (Not most prominent)

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Diagnostic Criteria: DSM-5[2]

- Major
  - Profound cognitive decline from baseline in ≥1 of the following
    - Complex attention, executive function, learning and memory, language, perceptual-motor, or social cognition
  - Decline interferes with independent activities
  - Cannot occur in the context of delirium or other psychiatric disorder
- Minor
  - Modest impairment from baseline in one of the six
  - Decline does not interfere with everyday activities
  - Cannot occur in the context of delirium or other psychiatric disorder

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Pharmacological Therapy[1]

Mild-Moderate AD	Moderate-Severe AD	Disease Worsens
Start acetylcholinesterase inhibitor (donepezil, rivastigmine, galantamine)	Start acetylcholinesterase inhibitor (donepezil, rivastigmine, galantamine) and/or memantine	Combination treatment: acetylcholinesterase inhibitor + memantine

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Acetylcholinesterase Inhibitors

- **MOA:** inhibit centrally-active acetylcholinesterase, the enzyme responsible for hydrolysis of acetylcholine, thereby causing an increase in acetylcholine

Drug	Dosing
Donepezil (Aricept) ODT, tablet + memantine (Namzaric)	Start: 5 mg QHS, can increase to 10 mg QHS after 4-6 weeks Moderate to severe: can increase to 23 mg QHS after ≥ 3 months of 10 mg QHS

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Acetylcholinesterase Inhibitors

Drug	Dosing
Rivastigmine (Exelon) Capsule, patch	Capsule: start 1.5 mg BID, can increase every 2 weeks to 6 mg BID Patch: start 4.6mg/24hrs, can increase every 4 weeks to 13.3 mg/24 hrs Hepatic impairment: max patch dose 4.6 mg/24 hrs
Galantamine (Razadyne, Razadyne ER) Table, capsule, solution	IR tablet or solution: start 4 mg BID, can increase every 4 weeks to 12 mg BID ER capsule: start 8 mg QD, can increase every 4 weeks to 24 mg QD Severe hepatic/renal impairment: do not use

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Acetylcholinesterase Inhibitors

Warnings

- Cardiac effects, including bradycardia, syncope, QT prolongation
- Anorexia/weight loss
- Patients < 55 kg can have more nausea and weight loss
- Neuroleptic malignant syndrome and rhabdomyolysis (both rare)

Common Side Effects

- Nausea, diarrhea (both dose-related, transient), insomnia, decreased appetite, weight loss

Drug Interactions

- Caution with other drugs that can lower heart rate and with drugs that cause dizziness
- Drugs that have anticholinergic effects can reduce efficacy of AChEi
- AChEi can increase gastric acid secretion, therefore, use NSAIDs with caution

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NMDA Receptor Antagonist

- **MOA:** blocks NMDA receptors, which inhibits glutamate from binding and decreases abnormal neuron activation

Drug	Dosing
Memantine (Namenda, Namenda XR, Namenda Titration Pack) Tablet, capsule, oral solution + donepezil (Namzaric)	IR: Start with 5 mg PO QD; titrate weekly to 10 mg PO BID ER: start with 7 mg PO QD; titrate weekly to 20 mg PO QD Can switch IR 10 mg BID to ER 28 mg QD; begin ER the day after the last IR dose CrCl < 30 mL/min: max dose 5 mg PO BID (IR) or 14 mg PO QD (ER)

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NMDA Receptor Antagonist

Warnings

- Caution with drugs/condition that increase urine pH, which decreases clearance of drug
  - Drugs → acetazolamide, bicarbonate, or potassium citrate
  - Conditions → renal failure, vomiting, urinary tract infections

Common Side Effects

- Generally well-tolerated, can cause dizziness, confusion, headache, constipation, syncope

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Pop Quiz #2

Memantine, an NMDA receptor antagonist, is used in the treatment of Alzheimer's disease primarily to:

a. Reduce inflammation in the brain
b. Enhance acetylcholine production
c. Slow the progression of cognitive decline
d. Treat behavioral symptoms

27

Pop Quiz #2

Memantine, an NMDA receptor antagonist, is used in the treatment of Alzheimer's disease primarily to:

a. Reduce inflammation in the brain
b. Enhance acetylcholine production
c. Slow the progression of cognitive decline
d. Treat behavioral symptoms

28

Updates

29

Aducanumab (Aduhelm®)[3]

- **FDA approved for treatment of AD in 2021**
- **Classification:** anti-amyloid monoclonal antibody
- **MOA:** reduces Aβ plaques
- **Dosing:** intravenous infusion

Initial	Maintenance

• Based on actual body weight
  • 1 mg/kg every 4 weeks for infusions 1 & 2
  • 3 mg/kg once every 4 weeks for infusions 3 &4
  • 6 mg/kg once every 4 weeks for infusions 5 & 6
	• 10 mg/kg once every 4 weeks starting with infusion 7

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Aducanumab (Aduhelm®)

Significant Adverse Reactions

- Amyloid-related imaging abnormalities (ARIA)
  - ARIA-E → vasogenic edema and/or sulcal effusions (20% - 64%)
  - ARIA-H → superficial siderosis and microhemorrhages (15% - 19%)
  - Clinical symptoms → altered mental status, abnormal gait, confusion, delirium, disorientation, dizziness, focal neurologic deficits, headache, nausea, seizure, and visual disturbance
  - Dose-related

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Aducanumab (Aduhelm®)

Clinical Trials

EMERGE (n = 1638)	ENGAGE (n = 1647)
Objective Evaluated efficacy and safety in early AD **Design** Randomized, double-blind, placebo-controlled, global, phase 3 studies **Intervention** Randomly assigned 1:1:1 to receive aducanumab low dose (3 or 6 mg/kg target dose), high dose (10 mg/kg target dose), or placebo via IV infusion once every 4 week over 76 weeks **Primary Outcome** Change from baseline to week 78 on the Clinical Dementia Rating Sum of Boxes, an integrated scale that assesses both function and cognition (higher score indicating greater impairment)	

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Clinical Dementia Rating Scale[4]

Impairment	None 0	Questionable 0.5	Mild 1	Moderate 2	Severe 3
Memory	No memory loss or slight	Consistently slight forgetfulness	Moderate loss; marked for recent events	Severe loss; new material rapidly lost	Severe loss; only fragments remain
Orientation	Fully orientated	Fully orientated except for time relationships	Orientated only for place at examination	Disorientated with time and place	Orientated to person only
Judgement and Problem Solving	Solves everyday problems; judgement good	Slight impairment in judgement	Moderate difficulty in judgement	Severely impaired in judgement	Unable to make judgements, solve problems
Community Affairs	Independent function at usual level	Slight impairment in activities	Unable to function at all these activities	No pretence of independent function outside home	
Home and Hobbies	Life and interests well maintained	Interests slightly impaired	Mild but definite impairment	Only simple chores preserved	No significant function in home
Personal Care	Fully capable of self-care		Needs prompting	Requires assistance in dressing, etc.	Requires much help

Washington University CDR is a global assessment instrument that yields global and SOB scores

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Clinical Dementia Rating Scale

CDR	Staging
0	No cognitive impairment
0.5	Questionable or very mild dementia
1	Mild
2	Moderate
3	Severe

Sum of Boxes Range	Severity
0	Normal
0.5 – 4.0 • 0.5 – 2.5 • 3.0 – 4.0	Questionable cognitive impairment • Questionable impairment • Very mild dementia
4.5 – 9.0	Mild dementia
9.5 – 15.5	Moderate dementia
16.0 – 18.0	Severe dementia

- The CDR-Global score, determines dementia stage, rated from 0-3
- The SOB score is a continuous measure of dementia severity and ranges from 0-18

Brent, Robert. Applied Economics (2022)

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Aducanumab (Aduhelm®)

Clinical Trials

EMERGE (n = 1638)	ENGAGE (n = 1647)

Results
• Studies were stopped based on futility analysis of data pooled from the first ~50% of enrolled patients
• Most common adverse event → ARIA-E
• EMERGE
  • Primary endpoint met → difference of -0.39 for high-dose aducanumab vs placebo [95% CI, -0.69 to -0.09; p = 0.012; 22% decrease]
• ENGAGE
  • Primary endpoint NOT met → difference of 0.03 [95% CI, -0.26 to 0.33; p = 0.833; 2% increase]	

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Aducanumab (Aduhelm®)

Clinical Trial Controversy[5]

- Implementation of certain study protocols and the premature ending of both trials may have contributed to the discordant results, where the high dose treatment arm of EMERGE was the only one to demonstrate cognitive improvement
- Baseline demographics of both trials featured uneven racial and ethnic distribution
  - 70-80% Caucasian, 2-4% Hispanic or Latino, and 0.2-1% Black or African America
- 80% of participants at baseline were in the mild cognitive impairment stage of AD

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Lecanemab-irmb (Leqembi®)[6]

- **FDA approved for treatment of early AD with confirmation of elevated Aβ in June 2023**
- **Classification:** Anti-amyloid monoclonal antibody
- **MOA:** directed against aggregated soluble and insoluble forms of Aβ; reduces Aβ plaques
- **Dosing:** dosing based on actual body weight → 10 mg/kg Q2W intravenous infusion

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Lecanemab-irmb (Leqembi®)

Significant Adverse Reactions

- Amyloid-related imaging abnormalities (ARIA)
  - ARIA-E → vasogenic edema and/or sulcal effusions (10% - 13%)
  - ARIA-H → superficial siderosis and microhemorrhages (6% - 17%)
  - Dose-related

38

Lecanemab-irmb (Leqembi®)

Clinical Trial

Lecanemab in Early Alzheimer's Disease (Clarity)
Objective Determine the safety and efficacy of lecanemab in participants with early Alzheimer's disease
Design 18-month, multicenter, double-blind, phase 3 trial
Intervention Participants were randomly assigned in a 1:1 ratio to receive intravenous lecanemab (10 mg/kg of body weight every 2 weeks) or placebo
Primary Outcome Change from baseline at 18 months in the score on the Clinical Dementia Rating-Sum of Boxes

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Lecanemab-irmb (Leqembi®)

Clinical Trial

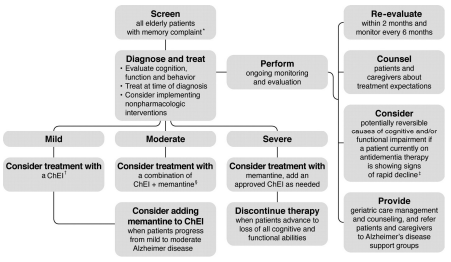
Lecanemab in Early Alzheimer's Disease (Clarity)

Results
Adjusted least-squares mean change from baseline at 18 months was 1.21 with lecanemab and 1.66 with placebo (difference, -0.45; 95% confidence interval [CI], -0.67 to -0.23; P<0.001)

Conclusion
Reduced markers of amyloid in early AD and resulted in moderately less decline on measures of cognition and function than placebo at 18 months but was associated with adverse events

40

Treatment Guideline Summary



Sadowsky CH, Galvin JE. *J Am Board Fam Med*. 2012.

41

Brexpiprazole (Rexulti®)[7]

REXULTI brexpiprazole 2mg tablets

- **FDA approved for treatment of agitation associated with dementia in patients with AD on May 10, 2023**
- **Classification:** second generation antipsychotic
- **MOA:** partial agonist activity of 5-HT1A and D2 receptors and antagonist activity for 5-HT2A receptors
- **Dosing:** 0.5 mg QD for 7 days, increase dose to 1 mg QD on days 8 to 14, then on day 15 to target dose of 2 mg QD

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Brexpiprazole (Rexulti®)

Adverse Reactions (>10%)

- Endocrine & metabolic → increased serum triglycerides (< 500 mg/dL: 8% to 28%; ≥ 500 mg/dL: < 1%), weight gain (≥ 7% increase in body weight: 2% to 11%)
- Nervous system: akathisia (1% to 14%)

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Brexpiprazole (Rexulti®)

Clinical Trial

Efficacy and Safety of Brexpiprazole for the Treatment of Agitation in Alzheimer's Dementia

Objective
Confirm the efficacy, safety, and tolerability of brexpiprazole in patients with agitation in Alzheimer dementia

Design
12-week, multicenter, randomized, double-blind, placebo-controlled trial

Intervention
- Study 1: brexiprazole fixed dose (1 mg/day and 2 mg/day) compared to placebo for a 12-week treatment period
- Study 2: brexpiprazole flexible dosing (0.5-2 mg/day) compared to placebo for a 12-week treatment period

Primary Outcome
Total CMAI score from baseline to week 12 of treatment

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Cohen-Mansfield Agitation Inventory

Cohen-Mansfield Agitation Inventory (CMAI)

Instructions: For each of the behaviors below, check the rating that indicates the average frequency of occurrence over the last 2 weeks.

Behavior	Never	Less Than Once a Week	Once or Twice a Week	Several Times a Week	Once or Twice a Day	Several Times a Day	Several Times an Hour
1. Hitting (including self)	☐	☐	☐	☐	☐	☐	☐
2. Kicking	☐	☐	☐	☐	☐	☐	☐
3. Grabbing onto people	☐	☐	☐	☐	☐	☐	☐
4. Pushing	☐	☐	☐	☐	☐	☐	☐
5. Throwing things	☐	☐	☐	☐	☐	☐	☐
6. Tearing things	☐	☐	☐	☐	☐	☐	☐
7. Screaming	☐	☐	☐	☐	☐	☐	☐
8. Spitting	☐	☐	☐	☐	☐	☐	☐
9. Hurt self or others	☐	☐	☐	☐	☐	☐	☐
10. Tearing things or clothing or hair	☐	☐	☐	☐	☐	☐	☐
11. Making physical or sexual advances	☐	☐	☐	☐	☐	☐	☐
12. Pacing, aimless wandering	☐	☐	☐	☐	☐	☐	☐
13. Inappropriate dress or undressing	☐	☐	☐	☐	☐	☐	☐
14. Trying to get to a different place	☐	☐	☐	☐	☐	☐	☐
15. Intentional falling	☐	☐	☐	☐	☐	☐	☐
16. Eating/drinking inappropriate substances	☐	☐	☐	☐	☐	☐	☐
17. Smearing or throwing inappropriately	☐	☐	☐	☐	☐	☐	☐
18. Hiding things	☐	☐	☐	☐	☐	☐	☐
19. Hoarding things	☐	☐	☐	☐	☐	☐	☐
20. Performing repetitious mannerisms	☐	☐	☐	☐	☐	☐	☐
21. General restlessness	☐	☐	☐	☐	☐	☐	☐
22. Screaming	☐	☐	☐	☐	☐	☐	☐
23. Making verbal sexual advances	☐	☐	☐	☐	☐	☐	☐
24. Cursing or verbal aggression	☐	☐	☐	☐	☐	☐	☐
25. Resisting bathing or getting dressed	☐	☐	☐	☐	☐	☐	☐
26. Strange noises (vocal laughter or crying)	☐	☐	☐	☐	☐	☐	☐
27. Complaining	☐	☐	☐	☐	☐	☐	☐
28. Negativism	☐	☐	☐	☐	☐	☐	☐
29. Constant unwarranted request for attention or help	☐	☐	☐	☐	☐	☐	☐

- 29-item scale to assess agitation
- Caregivers rate frequency with which, over the past two weeks, patients manifested physically aggressive, physically non-aggressive and verbally agitated behaviors
- Each item is rated on a 7-point scale ranging from "Never" to "Several times per hour"

https://www.apa.org/pi/about/publications/caregivers/practice-settings/assessment/tools/cohen-mansfield

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Brexpiprazole (Rexulti®)

Clinical Trial

Efficacy and Safety of Brexpiprazole for the Treatment of Agitation in Alzheimer's Dementia

Results

Study 1

- Primary: brexpiprazole 2 mg group showed statistically significant improvement in CMAI total score at week 12 unlike the 1 mg group compared to placebo

Study 2

- Primary: brexpiprazole 0.5-2 mg group did not achieve statistical superiority relative to placebo, however in a post hoc efficacy analyses for the subgroup of patients titrated to 2 mg at week 4 showed improvement in CMAI total score compared with similarly titrated placebo patients; for those not titrated to 2 mg (or equivalent placebo), there was no clinically meaningful separation

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Pop Quiz #3

Which of the following mechanisms is a key target in many of the latest Alzheimer's disease drug developments?

a. Increase tau protein production
b. Enhancing cholinesterase activity
c. Reducing beta-amyloid accumulation
d. Promoting neuroinflammation

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Pop Quiz #3

Which of the following mechanisms is a key target in many of the latest Alzheimer's disease drug developments?

a. Increase tau protein production
b. Enhancing cholinesterase activity
c. Reducing beta-amyloid accumulation
d. Promoting neuroinflammation

48

Future

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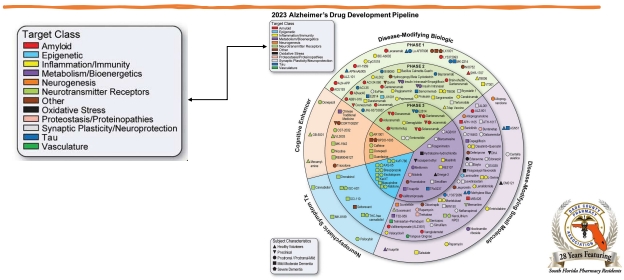
What's on the horizon?[8]



50

Donanemab (TRAILBLAZER ALZ 2)[9]

- **Not FDA approved**
  - Phase III clinical trial results were reported July 2023
- **Findings**
  - Randomized, multicenter, double-blind, placebo-controlled, 18-month, phase III trial with 1736 participants
  - Primary Outcome: Change in integrated Alzheimer Disease Rating Scale from baseline to 76 weeks
  - Study participants with early symptomatic Alzheimer disease, amyloid and tau pathology, treatment slowed clinical progression at 76 weeks

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Resources for Caregivers of Persons with AD

The following organizations provide educational literature and information on diagnosis, treatment, social support, and ongoing research in Alzheimer disease:

1. US Administration for Community Living, National Family Caregiver Support Program http://acl.gov/programs/support-caregivers/national-family-caregiver-support-program
2. National Institute on Aging (NIA) Alzheimer's Disease Education & Referral Center (ADEAR) http://www.nia.nih.gov.ezproxylocal.library.nova.edu/health/about-adear-center
3. Alzheimer's Association (AA) http://www.alz.org
4. Alzforum http://www.alzforum.org
5. Caregiver Action Network http://caregiveraction.org
6. Family Caregiver Alliance http://www.caregiver.org

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3. Budd Haeberlein, S., Aisen, P. S., Barkhof, F., Chalkias, S., Chen, T., Cohen, S., Dent, G., Hansson, O., Harrison, K., von Hehn, C., Iwatsubo, T., Mallinckrodt, C., Mummery, C. J., Muralidharan, K. K., Nestorov, I., Nisenbaum, L., Rajagovindan, R., Skordos, L., Tian, Y., van Dyck, C. H., … Sandrock, A. (2022). Two Randomized Phase 3 Studies of Aducanumab in Early Alzheimer's Disease. *The journal of prevention of Alzheimer's disease*, *9*(2), 197–210. https://doi.org/10.14283/jpad.2022.30
4. O'Bryant, S. E., Waring, S. C., Cullum, C. M., Hall, J., Lacritz, L., Massman, P. J., Lupo, P. J., Reisch, J. S., Doody, R., & Texas Alzheimer's Research Consortium (2008). Staging dementia using Clinical Dementia Rating Scale Sum of Boxes scores: a Texas Alzheimer's research consortium study. *Archives of neurology*, *65*(8), 1091–1095. https://doi.org/10.1001/archneur.65.8.1091
5. Brockmann, R., Nixon, J., Love, B. L., & Yunusa, I. (2023). Impacts of FDA approval and Medicare restriction on antiamyloidtherapies for Alzheimer's disease: patient outcomes, healthcare costs, and drug development. *Lancet regional health. Americas*, *20*, 100467. https://doi.org/10.1016/j.lana.2023.100467
6. van Dyck, C. H., Swanson, C. J., Aisen, P., Bateman, R. J., Chen, C., Gee, M., Kanekiyo, M., Li, D., Reyderman, L., Cohen, S., Froelich, L., Katayama, S., Sabbagh, M., Vellas, B., Watson, D., Dhadda, S., Irizarry, M., Kramer, L. D., & Iwatsubo, T. (2023). Lecanemab in Early Alzheimer's Disease. *The New England journal of medicine*, *388*(1), 9–21. https://doi.org/10.1056/NEJMoa2212948
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9. Sims JR, Zimmer JA, Evans CD, et al. Donanemab in Early Symptomatic Alzheimer Disease: The TRAILBLAZER-ALZ 2 Randomized Clinical Trial. *JAMA*. 2023;330(6):512–527. doi:10.1001/jama.2023.132

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Questions?

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Don’t Forget These – Updates in Alzheimer’s Treatments

Juhi Saxena, PharmD, M.S.
PGY-1 Pharmacy Resident
Mount Sinai Medical Center
Sunday, January 21, 2024

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Moving Forward: Innovations in Healthcare Technologies

Livia DeMello Lino, PharmD
Maria Albornoz, PharmD
University of Miami PGY-1 Residency Program
Miami, Florida
January 21th, 2023

28 Years Featuring
South Florida Pharmacy Residents

1

Objectives

- Describe the influence of pharmacogenomics on current pharmacy practice
- Review tele-pharmacy and its benefits on patient-centered care
- Assess current healthcare integration technologies

2

Pharmacogenomics

3

Pharmacogenomics

- Study of the role of the genome in drug response
- Goal is to enhance individualized medication therapy
- Genetic variations may affect drug-metabolizing enzymes, transporters, target proteins, and immune-related proteins
- Why is it useful?
  - Contraindications for specific genetic variants
  - Detection of enzymatic variants that decrease efficacy/increase toxicity
  - Selection of targeted treatment for specific mutations

Pirmohamed M. *J Clin Pharmacol*. 2001;52(4):345-347.a

4

History

- The term was defined by Friedrich Vogel of Heidelberg in 1959
- First recognized by Pythagoras in 510 BC with fava beans
- First drug linked to pharmacogenetics was succinylcholine in association with cases of prolonged paralysis in 1956
- First pharmacogenetic test approved in 2005 for alleles in CYP2D6 and CYP2C19 (hint: clopidogrel)

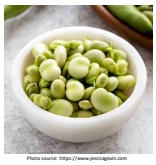

Photo source: https://www.jessicagavin.com

Squassina A, et al. *Pharmacogenomics*. 2010;11(8):1149-1167

5

Genetic Factors Influencing Drug Response

Pharmacokinetics
- CYP450 variants
- Thiopurines and TPMT/NUDT15 polymorphisms
- Drug transport

Pharmacodynamics
- VKORC1 and warfarin

Idiosyncratic reactions

Disease Pathogenesis

Tanaka E. *J Clin Pharm Ther*. 1999;24(5):323-329.

6

Diving Into the Benefits of Pharmacogenomics

- Improve time to effective treatment
- Reduce racial bias and undertreatment
- Reduce costs
- Reduce medication-related adverse effect

7

Improved Time to Effective Treatment

- An important component of personalized medicine

Prescription Medication Changes Following Direct-to-Consumer Personal Genomic Testing: The PGen Study

- Objective: to measure the frequency of prescription medication changes following direct-to-consumer personal genomic testing (DTC-PGT) and their association with the pharmacogenomic results received.
- Results:
  - Out of 961 subjects, 54 (5.6%) reported changing pharmacotherapy based on the genomic test results
  - 45/54 (83.3%) reported consulting with a health-care provider regarding the change
  - 91.2% received one or more atypical response results
  - The odds of reporting a prescription medication change increased 1.57 times (95% confidence interval = 1.17, 2.11)

Canera DA, et al. Genet Med. 2017;19(5):537-545.

8

Resources for Clinicians

The Clinical Pharmacogenetics Implementation Consortium (CPIC) (www.cpicpgx.org)
- Instructs on how pharmacogenomic testing can be integrated into clinical practice
- Does not provide recommendation if prospective testing should or should not be used to make treatment decisions in individual patients

FDA
- Table of pharmacogenetic association
- Pharmacogenetic associations for which the data support therapeutic management recommendations

Pharmacogenomics Knowledge Base (PharmGKB) (www.pharmgkb.org)
- Hosted by the NIH
- Database that consolidates pharmacogenomic data and guidelines recommendations

Sequence2Script (www.sequence2script.com/#/)
- Developed by the CPIC, the Dutch Pharmacogenetics Working Group (DPWG), and US Food & Drug Administration (FDA)
- Free online tool to help healthcare providers and clinical laboratories translate pharmacogenetic test results into clinically useful recommendations

9

Reduced Racial Bias and Undertreatment

- Genotyping for variants that affect drug metabolism can provide more accurate and less biased information than using surrogates such as race.

Race, Genotype, and Azathioprine Discontinuation: A Cohort Study

- Objective: to test whether rs2814778-CC gene was associated with azathioprine discontinuation attributed to hematopoietic toxicity and lower thiopurine dosing
- Results:
  - The rate of azathioprine discontinuation attributed to hematopoietic toxicity was 3.92 per 100 person-years among patients with the CC genotype (n = 101) and 1.34 per 100 person-years among those with the TT or TC genotype (n = 1365) (HR=2.92 [95% CI, 1.57 to 5.41])
  - The risk remained significant after adjustment for race (HR, 2.61 [CI, 1.01 to 6.71])

Dickson AL, et al. *Ann Intern Med.* 2022;175(8):1092-1099.

10

Reduce Medication Related Side Effects

A 12-Gene Pharmacogenetic Panel to Prevent Adverse Drug Reactions

Objective: to access the clinical utility of a pre-emptive genotyping strategy using a pharmacogenetic panel

Results:			
Adverse reactions	Intervention group (N=3342)	Placebo group (N=3602)	OR (95% CI)
Subjects with actionable mutations	152/725 (21%)	231/833 (27.7%)	0.7 (0.54-.91)
All patients	628/2923 (21.5%)	934/3270 (28.6%)	0.7 (0.61-0.79)

Swen JJ, et al. *Lancet.* 2023;401(10374):347-356.

11

Reduce Costs

- Some pharmacogenomic testing may reduce the costs of care

Cost-effectiveness of Pharmacogenomic-Guided Treatment for Major Depression Disorder (MDD)

- Objective:
  - To evaluate the effectiveness and cost-effectiveness of pharmacogenomic testing for MDD from the public payer's perspective over 20 years
- Results:
  - Modeling study suggested that implementation of a pharmacogenomic testing approach for individuals with major depressive disorder could save nearly $5000 USD per patient
  - Improved quality of life years by avoiding or slowing progression to refractory depression

Ghanbarian S, et al. *CMAJ.* 2023;195(44):E1499-E1508

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Challenges Into Application to Practice

- Study design limitations
- Regulatory and ethical concerns
- Lack of cost-effectiveness analyses
- Lack of tests and guidelines for test implementation
- Education in healthcare professional

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Challenges Into Application to Practice

- The Genetic Information Nondiscrimination Act (GINA) of 2008
  - Federal law that protects consumers from discrimination by health insurers and employers based on genetic information
  - Prohibits an insurer or employer from requesting or requiring that a person undergo a genetic test
  - Does not mandate coverage for any particular test or treatment

Hudson, et al. N Engl J Med. 2008;358(25):2661.

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Current Implementations

- Chemotherapy in cancer treatment (i.e. trastuzumab and lapatinib require FISH test)
- U.S. medical research institutions in the Electronic Medical Records and Genomics (eMERGE) Network
  - Vanderbilt University Medical Center – currently implementing PREDICT (Pharmacogenomic Resource for Enhanced Decisions in Care and Treatment)
  - Preemptive comprehensive pharmacogenetic test built in e-chart
  - Predicts up to 1 billion dollars reduction in healthcare expenses

Carlson B. *Biotechnol Healthc.* 2012;9(2):31-32.

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Current Available Pharmacogenomic Tests

- Herceptest®: measures HER2 protein to determine Herceptin treatment
- Amplichip®: CYP2D6 and CYP2C19
- DMET Plus Panel® and The PhyzioType®: several different SNP that are not available in standard labs
- PGxPredict:CLOZAPINE®: test for HLA-DQB1 gene

Squassina A, et al. *Pharmacogenomics*. 2010;11(8):1149-1167.

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Future of Pharmacogenomics

- As more robust data is published, the FDA will require genomic testing for diagnostic and drug therapy
- Main areas of research:
  - Combinatorial chemistry
  - Genomic mining
  - Omic technologies
  - High throughput screening
- As the cost per genetic test decreases, the development of personalized drug therapies will increase
- Technology now allows for genetic analysis of hundreds of target genes involved in medication metabolism and response in less than 24 hours for under $1000
- Non-prescription genomics tests: 24Genetics, ClarityX, and 23andMe

Paul NW, et al. *Curr Drug Targets*. 2006;7(12):1721-1727

17

ASSESSMENT

For which of the following drugs can the CYP2C19 pharmacogenomic test be used?

a. Ticagrelor
b. Prasugrel
c. Clopidogrel
d. Aspirin

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Tele-pharmacy

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Tele-pharmacy Overview

Tele-pharmacy is defined as the provision of pharmacist care by pharmacists and pharmacies by telecommunications to patients located at a distance

The service can include medication selection, order review and dispensing, patient counseling and monitoring and provision of clinical service

This practice can be adopted to provide a wide coverage of pharmaceutical services to underserved areas due to economic or geographic problems and sometimes, to address the problem of pharmacist shortage

Baldoni S, et al. *Medicina*. 2019;55(7):327.

20

Tele-pharmacy History

- Application of the information and communication technologies (ICTs) to the health care system have been opening new perspectives in the delivery of health services
- **Tele-medicine and Tele-pharmacy: Current Status and Future Implications**, published in 1999
  - Showing at that time, benefits of tele-pharmacy such as improved productivity and achievement of underserved areas
- New studies, such as **Tele-pharmacy Services: Present Status and Future Perspectives: A Review** published in 2019, shows the same benefits as previously mentioned, with the addition of the reduction of pharmacy services costs as one pharmacist can cover multiple sites, with the use of technology

Baldoni S, et al. *Medicina*. 2019;55(7):327.
Angaran, D. AJHP. 1999. 56 (1405-1426)

21

Advantages of Tele-pharmacy

- Remote dispensing (retail/outpatient/inpatient)
- Remote patient counseling, reaching underserved areas, assessing duplications, adherence and possible adverse reactions
- Remote order-entry review, overcoming pharmacist shortage

https://blog.curvatc.com/6-of-the-top-benefits-of-telepharmacy

Baldoni S, et al. *Medicina*. 2019;55(7):327.

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Potential Disadvantages of Tele-pharmacy

- Decreased human interaction between health professionals and patients
- Possible problems in the evaluation of drug dispensing
- An increased risk for security and integrity of patient data
- Financial investment to technology
- Elderly patients may find it more difficult and harder to access

Baldoni S, et al. *Medicina*. 2019;55(7):327.

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Financial Investment

- The success of tele-pharmacy services depends to the level of technological infrastructures, such as efficient internet connections
  - The lack of good technological standards can prevent a proper service delivery
- A secure service is needed for the protection and encryption of patient information to avoid data leaking
- The acquisition of software and devices may be a financial burden that small healthcare centers cannot afford

Baldoni S, et al. *Medicina*. 2019;55(7):327.

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Cost Reduction

- At the same time an investment is needed, the introduction of tele-pharmacy services can bring to a reduction of pharmacy services costs:
  - One pharmacist can cover multiple sites and a wider area that otherwise would require a higher number of pharmacists
  - Patients in rural areas can be reached by tele-pharmacy
- Tele-pharmacy allows patients to save money and travel time, which are the major problems encountered, especially by elderly patients, to reach healthcare structures

Baldoni S, et al. *Medicina.* 2019;55(7):327.

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Reduction in Medication Errors

- Medication errors contribute to 250,000 nonfatal injuries and 7000 deaths every year in the United States, and the annual cost of preventable adverse drug events averages approximately 2 billion US dollars
- In many hospitals, the implementation of tele-pharmacy services has led to a decrease of medication errors rates
  - **Current Practices and State Regulations Regarding Tele-Pharmacy in Rural Hospitals**, a practice report published in 2001 in rurales hospitals in Illinois
  - Showed a decrease in medication errors, when utilizing tele-pharmacy to overcome pharmacist shortage
- Increasing pharmacist interventions can prevent not only medication errors, but also prevent medication-related events as side-effects and drug interactions promoting an individualized patient care

Baldoni S, et al. *Medicina.* 2019;55(7):327.
Casey M, et al. AJHP. 2010; 67 (1085-1092).

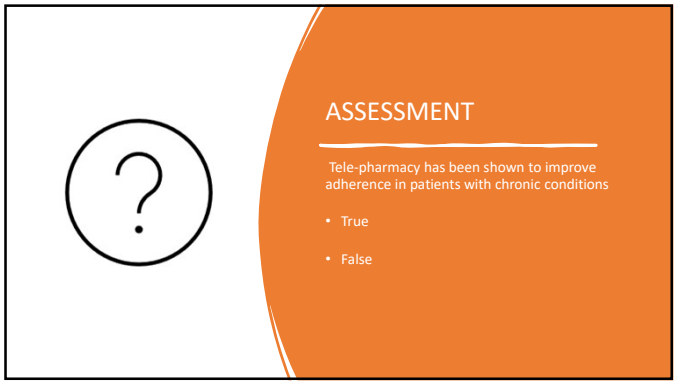
26

Prevention of Non-adherence

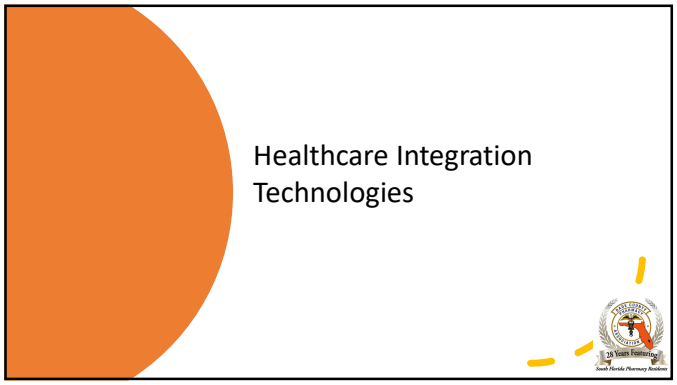
- Non-adherence puts an additional expenditure burden for rehospitalization of US $100 to US $290 billion a year in the United States
- Tailored patient counseling that targets the underlying causes of non-adherence is one method of helping patients to improve their medication-taking behaviors
- Focused counseling and monitoring of patients can help to decrease this additional expenditure

Maspan, C. The Pharmacist, 2019.

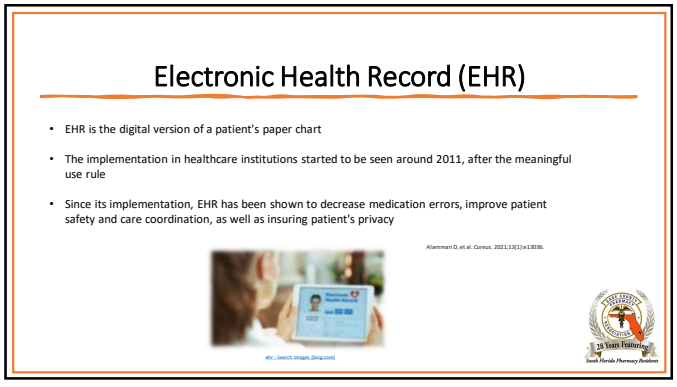
27


ASSESSMENT
Tele-pharmacy has been shown to improve adherence in patients with chronic conditions
• True
• False

28


Healthcare Integration Technologies

29


Electronic Health Record (EHR)
• EHR is the digital version of a patient's paper chart
• The implementation in healthcare institutions started to be seen around 2011, after the meaningful use rule
• Since its implementation, EHR has been shown to decrease medication errors, improve patient safety and care coordination, as well as insuring patient's privacy
Alammari D, et al. Cureus. 2021;13(1):e13036.

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Healthcare Integration Technologies

MEANINGFUL USE

INTEROPERABILITY

BARCODES AND RFID TECHNOLOGY

31

Meaningful Use History

- Electronic health record (EHR) incentive program
- The goal was to improve quality, safety and efficiency of healthcare EHR technology, using incentive payments through the Centers for Medicare & Medicaid Services EHR Incentive Programs, for the qualifying hospitals and providers
- Originally launched in 2011 by the U.S government
- Required eligible providers and hospitals to use electronic health record (EHR) for data capture and sharing

Alammari D, et al. *Cureus*. 2021;13(1):e13036.
Lehne M, et al. *NPJ Digit Med*. 2019. 20;2:79.

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Meaningful Use Pillars

1. Improving quality, safety, and efficiency while reducing health disparities
2. Engaging patients and families
3. Improving care coordination
4. Improve public health
5. Ensure privacy for personal health information

Alammari D, et al. *Cureus*. 2021;13(1):e13036.

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Stages of Meaningful Use

Stage 1 (2011-2012): promoting EHR adoption, with data capture and sharing

Stage 2 (2014): encourage the use of EHRs for increased exchange information and continuous quality improvement at the point of care

Stage 3 (2016): changes were made to reduce the complexity of the measures, with many objectives carried from stage 2, focusing on improvement of healthcare outcomes

Alammari D, et al. *Cureus*. 2021;13(1):e13036.
Lehne M, et al. *NPJ Digit Med*. 2019. 20;2:79.

EHR: Electronic health record

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Meaningful Use Benefits

With the implementation of meaningful use, more opportunities were brought to healthcare-systems, such as:

- Improvement in patient safety with the decrease of medication errors
- Protection of personal information, with the use of safer and appropriate systems
- Better communication between healthcare providers and pharmacies
- Providing access to patient's medical history anywhere

Alammari D, et al. *Cureus*. 2021;13(1):e13036.
Lehne M, et al. *NPJ Digit Med*. 2019. 20;2:79.

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Healthcare Integration Technologies

MEANINGFUL USE

INTEROPERABILITY

BARCODES AND RFID TECHNOLOGY

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Interoperability

- Interoperability is defined as the ability of **two or more** systems or components to exchange information and to use the information that has been exchanged (e.g.: CAPS – Epic)
- Interoperability is the future of pharmacy as new technologies are being developed allowing the interface between systems
- Having systems that interface and communicate with each other can offer a safer environment for patients and more effective for healthcare employees

Alammari D, et al. *Cureus*. 2021;13(1):e13036.
Lehne M, et al. *NPJ Digit Med*. 2019. 20;2:79.

CAPS®: A registered trademark of Central Admixture Pharmacy Services, Inc.

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Interoperability Benefits

1. Cost reduction/Improved productivity

- Achieving interoperability enables healthcare organizations to utilize pharmacists on tasks that directly reduce healthcare costs and improve quality
- Time-consuming manual processes, such as data entry and managing mismatched or unmatched patient records can be eliminated
- Allows for a faster and smoother data exchange, decreasing the length of stays due to delays in information transfer

Kyrylo, Lusov. Interoperability in Healthcare. Jelvix. 2022.

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Interoperability Benefits

2. Improve patient safety

- Interoperability guarantees a high level of data accuracy by eliminating human factors and limiting the risks of mistakes
- Data entry errors often lead to duplicate medical records, duplicate tests/exams, and other inefficiencies that cost healthcare organizations time and money
- Eliminating the need for manual data entry helps minimize burnout and reduce the possibility of medical errors

Alammari D, et al. *Cureus*. 2021;13(1):e13036.
Lehne M, et al. *NPJ Digit Med*. 2019. 20;2:79.

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Interoperability Benefits

3. Patient access to data

- Health records became readily available to patients
- Facilitates patient's access to their complete history of prior treatment, medications, and procedures
- Providers and patients gain timely and secure access to health records regardless of the system or geographical locations

What is Interoperability: The Future of Clinical Interoperability in Healthcare [article.com]

Kyrylo, Lusov. Interoperability in Healthcare. Jelvix. 2021.

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Barriers of Interoperability

1. Lack of administrative IT support

- Pharmacist role in clinical informatics was first defined by ASHP in 2016
- Clinical informatics pharmacists play a key role in maintaining the data, information, and knowledge assets across all systems that support medication management
- Contribute to the transformation of healthcare by analyzing, designing, implementing, maintaining, and evaluating information and communication systems that improve medication-related outcomes and strengthen the pharmacist– patient relationship

Alammari D, et al. *Cureus*. 2021;13(1):e13036.
Lehne M, et al. *NPJ Digit Med*. 2019. 20;2:79.

IT: Information technology

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Barriers of Interoperability

2. Lack of Consistency of Healthcare Standards

- Health care organizations sometimes use different systems lacking a single standard system for data exchange
- Some systems, cannot interpret the exchanged information properly
- This fact can make interoperability harder and more expensive to be implemented as conversion of data or new system implementation may be needed

Alammari D, et al. *Cureus*. 2021;13(1):e13036.
Lehne M, et al. *NPJ Digit Med*. 2019. 20;2:79.

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Barriers of Interoperability

3. High Implementation Costs

- Cost of implementing all standards and building customized interfaces may become a barrier, especially for smaller institutions
- Achieving healthcare interoperability often requires developing and optimizing multiple interfaces that must work with several different systems
- Estimations show that the cost of interoperability implementation and maintenance can reach about $1.6 million per healthcare organization

Alammari O, et al. Cureus. 2021;13(1):e13036.
Lehne M, et al. *NPJ Digit Med.* 2019. 2(2):79.

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ASSESSMENT

Can CAPS be integrated with EHR interface?

- True
- False

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Healthcare Integration Technologies

MEANINGFUL USE

INTEROPERABILITY

BARCODES AND RFID TECHNOLOGY

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Barcodes Overview

- Barcodes started to gain significance, given the fact that 35 % of the medication errors happen at the administration stage
- In 2005, a study published on barcoding reducing errors, showed that errors were being reduced by 82% with the use of barcodes, also reducing harmful impact to patients
- In 2007, the annual Healthcare Information and Management Systems Society (HIMSS) survey identified barcode specimen systems as **the number one priority** for reducing medical errors and improving patient safety

Thompson KM, et al. Mayo Clin. 2018;2(4):342-351.

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RFID Technology

- A wireless technology that uses radio waves for data collection and transfer from an electronic tag attached to an object or person
- Data is captured efficiently, automatically and in real time without human intervention, enabling automatic identification of objects
- RFID technology have been successfully applied to the areas of manufacturing, supply chain, agriculture, transportation and healthcare

Ajami S, et al. J Res Med Sci. 2013;18(9):809-813.

RFID: Radio-Frequency Identification technology

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Benefits of RFID Technology

- Inventory tracking
- Monitoring of patients
- Can further reduce the risk of administering the wrong medication, increasing patient safety
- Tracking of nurses and patients
- Improves communications between caregivers

Ajami S, et al. J Res Med Sci. 2013;18(9):809-813.

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Barriers of RFID Technology

- Privacy concerns as data leakage with data being retrieved from a distance
- Funding for initial application of the technology
- Staff training at implementation
- Continuous internet requirements
- High electricity demands

Ajami S, et al. J Res Med Sci. 2013;18(9):809-813.

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Barcode vs RFID Technology

- When comparing barcodes to RFID technology, they are both efficacious in preventing medication errors and securing the 5 rights (right patient, right drug, right time, right dose, and right route)
- However, RFID technology contains a unique identifier, that can be used to identify a single RFID tag out of a group of RFID tags, in contrast to barcode system where the barcode represents the serial number of the item but is not unique
- Barcodes must be individually read whereas groups of RFID tags can be read simultaneously

Ajami S, et al. J Res Med Sci. 2013;18(9):809-813.

RFID: Radio Frequency Identification technology

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Questions?

Thank you!

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Veterinary Medicine:
What Pharmacists Need Know

Dairene Leon, Pharm. D.
PGY-1 Pharmacy Resident
Baptist Hospital of Miami
January 2024

28 Years Featuring
South Florida Pharmacy Residents

1

Objectives

1. Define the role of the pharmacist in veterinary medicine
2. Discuss laws and regulations that affect the practice of veterinary pharmacy
3. Describe pharmacotherapy options for veterinary patients

2

Background

3

Pet Medications: A Growing Market

- Pets are found in ~85 million homes in the US
- 95% of pet owners consider their pet to be a member of the family
- Americans spent $136.8 billion on their pets in 2022, up 10.68% from 2021
- Drug sales for dogs and cats reached $12 billion in 2022, representing a continuing upward trend

American Veterinary Medical Association, 2018 and 2022 Pet Ownership and Demographics Sourcebook

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Trends in Veterinary Prescribing

- Increased outsourcing of animal prescriptions

Animal medications were only available from the prescribing veterinarian's clinic	Pet owners are increasingly seeking competitive pricing for pet medications	Convenience of filling the entire family's prescriptions in one pharmacy

- Benefit in outsourcing prescriptions
  - Decreasing drug inventory ↓ costs

American Pet Products Association, Pet industry market size and ownership statistics.

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Understanding Vet Prescriptions

- Different terminology and abbreviations
- Key details:
  - Pet owners → "clients"
  - Pets → patients
  - Use of abbreviations is common
    - SID → once a day
      - Has been misread by pharmacists as 4 or 5 times a day, which can result in dangerous overdoses
  - Oral liquids are rarely prescribed as per 5 mL
    - Amoxicillin 250 mg/5 mL suspension is commonly prescribed as 50 mg/mL

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Role of the Pharmacist

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Role of the Pharmacist

Community pharmacists **will** be presented with a veterinary prescription

- The pharmacist is in a unique position to serve both the animal patient and their human caregiver
- Knowing how to accurately verify the prescription, appropriately support the veterinarian, and comprehensively counsel the pet owner is imperative for therapeutic success
- Pharmacists may perceive these radically different doses as mistakes

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Pharmacists' Knowledge of Veterinary Pharmacotherapy and the Impact of an Educational Intervention

Objectives	Assess pharmacists' baseline knowledge of veterinary pharmacotherapy, as relevant to the profession, and assess the impact of a piloted educational program
Methods	• A statewide assessment of pharmacists' knowledge of veterinary pharmacotherapy • Educational intervention to improve pharmacists' veterinary pharmacotherapy knowledge base • Participants were assessed via pretest and posttest
Results	• N = 602 received a mean score of 5.9 (SD = 2.6) on a 17-item questionnaire • No differences in participants' knowledge based on subject matter of the question • Using the same 17-item questionnaire, pilot study participants (n = 60) received a mean score of 5.2 (SD = 2.4) on the pretest and 16.6 (SD = 0.7) on the posttest
Conclusion	• Many pharmacists lack the knowledge needed to process and dispense the veterinary prescriptions most encountered in community pharmacies • Implementation of an educational intervention can increase pharmacists' knowledge of core concepts necessary to safely care for animal patients

Young NW et al. Pharmacists' Knowledge of Veterinary Pharmacotherapy and the Impact of an Educational Intervention. J Pharm Technol. 2018;34(6):244-251

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Laws and Regulations

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Veterinary Prescription Requirements

Veterinarian's name, address, and telephone	Client's name, address, and telephone	Animal ID (name, species)
Drug name, strength, formulation and quantity	Directions for use	Specific cautionary statements
Withdrawal times (if applicable)	Prescriber signature	Date issued

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Human Prescription Requirements

Name of the prescriber	Name and strength of the drug prescribed	Quantity of the drug prescribed
Directions for use	Date written	Prescriber signature

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Veterinary Label Requirements

Veterinarian's name, address, and telephone	Client's name	Animal ID (name, species)
Drug name, strength, formulation and quantity	Directions for use	Specific cautionary statements
Date of original Rx, dispensing, and drug and refill expiration	Withdrawal times (if applicable)	Federal transfer warning, if controlled substance

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Human Label Requirements

Pharmacy name and address	Date of dispensing	Serial number (prescription number)	Name of the patient
Name of the prescriber	Name of the drug	Directions for use	Expiration or beyond-use date
		Federal transfer warning, if controlled substance	

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Veterinary Medical Mobility Act (2014)

Amendment to Controlled Substances Act

- Allows veterinarians to carry and dispense controlled substances beyond primary DEA-registered location
- Licensed veterinarians can hold controlled substances registrations in multiple states, regardless of location of principal place of business

Veterinary Medicine Mobility Act of 2014, H.R. 1528

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Extra-Label Drug Use (ELDU)

- Use of pharmaceutical drugs for unapproved situations
  - Indications
  - Dosages and frequencies
  - Age groups
  - Formulations
  - Route of administration
  - Species

Animal Medicinal Drug Use Clarification Act, 21 CFR 530

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Animal Medicinal Drug Use Clarification Act

- Legalized extra-label drug use in animals
- Key constraints:
  - "ELDU" must be by or on the order of a veterinarian
  - ELDU must not result in violative residues in food-producing animals
  - ELDU not allowed in animal feeds
  - Requires accurate recordkeeping and labeling practices
  - May limit use in non-food animals if there is a public threat

Animal Medicinal Drug Use Clarification Act, 21 CFR 530

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General Conditions for ELDU

- No animal drug approved for the intended use
- An approved drug for the intended use exists, but not in the required dosage form or concentration
- Approved drug has been found to be clinically ineffective for labeled indication
- If intended use is in a non-food animal, an approved human drug can be used even if an approved animal drug is available

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Restrictions for ELDU in Food Animals

- Must have medical rationale for ELDU
- Ensure assigned withdrawal times are met and no illegal residues occur
- Food Animal Residue Avoidance Databank for withdrawal intervals; if not available, treated animals must not enter human food supply
- Carefully record/track animal IDs
- Use of approved human drugs in food-producing animals is not permitted if an approved animal drug can be used

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Compounding

- Considered a form of ELDU that must be done from approved finished dosage forms
- Compounded drugs should not be used if an approved drug is available in the desired dose and dosage form
- Compounding from a human drug for use in food-producing animals will not be permitted if an approved animal drug can be used

Animal Medicinal Drug Use Clarification Act, 21 CFR 530

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Compounding

Veterinarians and pharmacists are **NOT** allowed to compound **unapproved** finished new animal drug products from bulk pharmaceuticals

Example: pergolide (human-labeled Permax) used to treat Parkinson's disease

- Withdrawn from U.S. market in 2007 due to valvular heart disease
- Used in Equine Cushing's Syndrome
- Compounded from bulk pharmaceuticals until 2012 when Prascend was introduced

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Prohibited Drugs in Food-Producing Animals

Drug	Reason for Prohibition
Diethylstilbestrol (DES)	Associated with cancer
Nitroimidazole class	
Nitrofuran class	
Sulfonamide class (in lactating dairy cattle)	
Chloramphenicol	Toxic reactions
Clenbuterol	
Phenylbutazone(in female dairy cattle ≥20 months of age)	
Fluoroquinolone class	Antimicrobial resistance
Vancomycin	

UC Davis Veterinary Institute for Food Safety & Security. Livestock Drug Safety: Prohibited Drugs

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Additional Restrictions

Cephalosporins in cattle, swine, chickens, or turkeys

- Not approved for species and production class
- Unapproved doses, frequencies, durations, or routes of administration
- For disease prevention

Drug classes for treating or preventing influenza A in chickens, turkeys, and ducks

- Adamantanes
- Neuraminidase inhibitors

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Question #1

True/false: Veterinary prescriptions may not be filled for any extra-label (off label) drug use indication.

True | False

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Question #1

True/false: Veterinary prescriptions may not be filled for any extra-label (off label) drug use indication.

True	**False**

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Pharmacotherapy

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Pharmacokinetic/Pharmacodynamics

Dogs	Cats
• ~30% more blood/kg, affecting drug concentrations • Faster glomerular filtration rate, more rapid renal elimination • Faster GI transit time, some extended-release formulations may not have adequate time within the GI tract to release the medication	• Deficient or limited in several metabolic pathways, including hepatic glucuronidation, hydroxylation, and demethylation • May use different hepatic CYP isoenzymes to metabolize drugs

Riviere JE, Papich MG. Veterinary Pharmacology and Therapeutics. 9th ed. Ames, IA: Wiley-Blackwell; 2009

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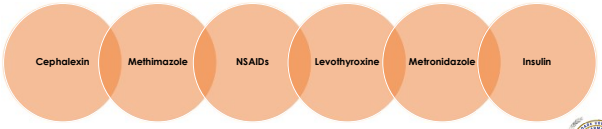
Commonly Prescribed Drugs

- Most prescribed medications for pets dispensed in the community setting



Ciccone C. Veterinary Medicine in Community Pharmacy. Pharmacy Times

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Cephalexin Clinical Pearls

- Only available as human-labeled products
- Often prescribed over veterinary-specific antibiotics due to cost
- Oral dosage forms may cause gastrointestinal effects such as vomiting or diarrhea
- Cephalexin can be given with food to avoid or reduce stomach upset
- Adverse reactions are rare and mild

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Methimazole Clinical Pearls

- Contraindicated in liver disease, autoimmune disease, or concurrent hematologic abnormalities
- Does not cure thyroid disease and will only decrease the amount of thyroid hormone in the body
- Tablets should be stored at room temperature in light-resistant containers

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NSAIDs Clinical Pearls

- Carprofen is indicated to treat acute pain and inflammation
- OTC NSAIDs should be avoided due to high toxicity in both dogs and cats
  - Potential for renal failure, gastric ulcerations, and perforations
  - For example, ibuprofen is contraindicated in both cats and dogs due to increased sensitivity to adverse effects at therapeutic doses

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Metronidazole Clinical Pearls

- Used for parasitic and anaerobic infections
- Only available as human-labeled products
- Administered either as an injection or orally
- Absorption of metronidazole is enhanced by food
- Metallic taste makes some oral dosage forms unpalatable
  - Capsules or compounded suspensions are preferred

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Levothyroxine Clinical Pearls

- Used in dogs for hypothyroidism
- Dogs receive a starting dose of 18 to 22 mcg/kg orally twice a day
  - Much higher than a human dose due to higher clearance and lower bioavailability of the drug in canines
- High-fiber pet food may reduce absorption of levothyroxine

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Gabapentin

- Anti-seizure and pain medication
- Also used in cats to treat fear and anxiety associated with veterinary visits
- Most common side effects include sedation (sleepiness) and incoordination
  - Can be worse the first time the pet is given the medication
  - Side effects generally go away within 24 hours
  - Gradual increases of the medication over time is recommended
- Recommended doses: 5 mg q 12 hours to 10 to 30 mg q 8 hours
- **Do not give the oral liquid form made for humans**

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Fluoxetine

- Aids in the management of anxiety and depression
- May also be prescribed for behavior issues, obsessive compulsive disorder, anxiety, digestive issues, and inflammatory bowel disease
- FDA approval for canine separation anxiety
- Recommended dose of Fluoxetine will depend on size and severity of symptoms
- Most common side effects include sleepiness and decreased appetite

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Administration of Oral Medications

Pills, Capsules, Tablets

1. Hold the drug between thumb and index finger of dominant hand
2. With the other hand, firmly grip the upper jaw using the thumb and index finger
3. Use your middle finger of the same hand to open lower jaw and tilt head upwards
4. Pop the medicine as far back on the tongue as possible and close pet's mouth

Liquid Medications

1. Fill the dropper and hold in dominant hand
2. Kneel beside pet on the same side as your dominant hand
3. Take your other hand and place it behind the dog's head
4. Next, put the tip of the dropper into the side of pet's mouth
5. Drain the dropper and release animal once empty

Tips

1. Hide in food
2. Administer during distractions

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Insulin Clinical Pearls

- Main treatment for diabetes
- Can use human insulin products and veterinary insulin products
- Vetsulin is a veterinary porcine insulin product
  - Canine insulin is more similar to porcine insulin than human insulin
  - Not available in most retail pharmacies
  - Pharmacists should be aware that its concentration is 40 U/mL and that it requires a U-40 syringe
  - Cats may be prescribed Vetsulin, but are more commonly prescribed insulin glargine

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Insulin Administration Pearls

- Ideal administration time is while or after eating
- Do not swab area prior to administration
- Lift a stretchy area of pet's skin – easiest over the shoulders but should rotate sites!

Behrend et al., 2018 AAHA Diabetes Management Guidelines for dogs and cats, 2018

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Monitoring Blood Glucose

Blood Glucose Curves (BGCs) are recommended

- Measure BG **q 2 hr** for one interval between injections
- BG should be monitored **every 3–4 hr** if using insulin glargine

A BGC should be performed:

1. After the first dose of a new kind of insulin
2. At 7–14 days after an insulin dose change
3. At least q 3 mo even in well-controlled patients
4. Any time clinical signs recur in a controlled patient
5. When hypoglycemia is suspected

BGCs can vary from day to day when done at home and must always be interpreted in consideration of clinical signs

Suggested Prick Sites

Behrend et al., 2018 AAHA Diabetes Management Guidelines for dogs and cats, 2018

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Monitoring Blood Glucose

- Most accurate glucometer → AlphaTrak 2
- Calibrated for dogs and cats
- Human glucometers are not recommended due to reading inaccuracies

The **ideal nadir is a BG of 80–150 mg/dL**. The **highest BG** should be close to **200 mg/dL in dogs** and **300 mg/dL in cats**

Behrend et al., 2018. AAHA Diabetes Management Guidelines for dogs and cats. 2018

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Continuous Glucose Monitoring (CGM) System

- FreeStyle Libre (FSL) measures interstitial glucose concentration q 15 min for up to 14 days
- Generally accurate, but some discrepancies between the FSL and AlphaTrak 2 in in patients with low glucose readings
- Clients should be aware that sensors do not always stay functional and attached for the full 14 days, but the information gained from even a few days of use is usually more helpful than a single BGC

Behrend et al., 2018. AAHA Diabetes Management Guidelines for dogs and cats. 2018

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Clinical Signs of Hypoglycemia

Lack of appetite	Lack of energy or lethargy	Shivering or shaking	Loss of coordination or weakness
Disorientation or stupor	Vomiting	Tremors or seizures	Fainting, loss of consciousness, or coma

Behrend et al., 2018. AAHA Diabetes Management Guidelines for dogs and cats. 2018

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Over the Counter (OTC) Medications

- Temporary relief of clinical signs for minor medical problems or serve as maintenance therapy for chronic conditions
- Many are not safe to use → toxic, fatal
- Should not be used for more than 1-3 days without consulting a veterinarian

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Question #2

True/false: A pharmacist may provide OTC recommendations for short-term use in animals without consulting a veterinarian.

True	False

44

Question #2

True/false: A pharmacist may provide OTC recommendations for short-term use in animals without consulting a veterinarian.

True	False

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Antihistamines

- Mainly used for treatment of allergy signs
- First generation antihistamines also work to prevent motion sickness and as antiemetics

Drug	Dogs	Cats
Diphenhydramine (Benadryl)	2-4 mg/kg PO q8h	
Cetirizine (Zyrtec)	5-10 mg PO q12h or q24h	2.5-5 mg PO q12h or q24h
Loratadine (Claritin)	0.5 mg/kg PO q24h	
Meclizine (Antivert)	4 mg/kg PO q24h	

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Topical Medications

Clean and dry affected area

Use an e-collar

Not recommended for prolonged use

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Topical Medications

Corticosteroids	Hydrocortisone 1% (Cortizone-10)	Apply 1-4 times daily until controlled, then taper
Antibiotics	Bacitracin, Neomycin, and Polymyxin B (Neosporin)	Apply 1-3 times daily for 1-3 days
	Bacitracin and Polymyxin B (Polysporin)	
Antifungals	Clotrimazole 1% (Lotrimin AF)	Apply twice daily for 2-4 weeks
	Terbinafine 1% (Lamisil AT)	Apply twice daily for 1-2 week

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Loperamide (Imodium)

- Used to control diarrhea
- Do not give to certain herding breeds (i.e. Shelties, Collies, Australian Shepherds)
- Dogs
  - 0.08 mg/kg PO **q8h**
- Cats
  - 0.08 mg/kg PO **q12h**
  - Tends to be avoided due to potential excitatory behavior
- Oral liquid is formulation of choice

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H2 Receptor Antagonists

- Treatment and prevention of stomach and intestinal ulcers and erosions
- Most OTC use related to gastritis
- Famotidine (Pepcid AC)
  - Dogs and Cats: 0.5-1 mg/kg PO q12h or q24h

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CBD Products

- Anecdotal evidence from pet owners suggesting CBD products can help with:
  - Anxiety
  - Pain, especially neuropathic pain
  - Controlling seizures
- However, more research with different CBD products and dosages is necessary to understand efficacy

Wakshlag JJ, et al. Cannabinoid, Terpene, and Heavy Metal Analysis of 29 Over-the-Counter Commercial Veterinary Hemp Supplements. Vet Med (Auckl). 2020;11:45-55.

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Cannabinoid, Terpene, and Heavy Metal Analysis of 29 Over-the-Counter Commercial Veterinary Hemp Supplements

Objective	Review plant constituents including cannabinoids, terpenes and heavy metal contamination (lead, arsenic, mercury and cadmium) in commercial products
Methods	• Analyzed 29 supplements for dogs that were using low-THC *Cannabis sativa* extracts • All products tested for cannabinoids, terpenes and heavy metals
Results	• Products were below the federal limit (0.3% THC) with variable amounts of CBD • Two products did not supply a CBD or total cannabinoid concentration, while 22 could supply a certificate of analysis (COA) from a third-party laboratory • Ten products were measured to have a total cannabinoid concentration that was within 10% of the amount that they claimed to have on their label • Heavy metal contamination was found in 4/29 products, with lead being the most prevalent contaminant (3/29)
Conclusion	• Only18 of 29 being appropriately labeled according to current FDA non-medication, non-dietary supplement or non-food guidelines • Owners and veterinarians wanting to utilize CBD-rich *Cannabis sativa* products should be aware of low-concentration products and should obtain a COA enabling them to fully discuss the implications of use and calculated dosing before administering to pets

Wakshlag JJ, et al. Cannabinoid, Terpene, and Heavy Metal Analysis of 29 Over-the-Counter Commercial Veterinary Hemp Supplements. Vet Med (Auckl). 2020;11:45-55.

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Toxicities and Adverse Effects

Acetaminophen	Fatal methemoglobinemia in cats
Doxycycline	Can cause esophageal erosions and strictures when dry-pilled in cats
NSAIDS	Serious GI bleeding and/or renal toxicity in cats and dogs
Permethrin	Fatal to cats
Phenobarbital	Hepatotoxicity in dogs
Tea tree oil	Toxicosis post oral or dermal exposure to 100% oil
Xylitol	Found in some liquid formulations of gabapentin; life-threatening hypoglycemia and acute hepatic failure in dogs

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Hydrogen Peroxide 3%

- Induces vomiting
- Dogs and Cats
  - 1 mL/1 lb orally, repeat in 15 minutes if no effect, not to exceed 3 doses
- Very fast-acting, very safe, very effective at causing emesis
- **Every pet owner should have at home!**

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Poison Control

Poison Control

- Phone number: (800) 222-1222

American Society for the Prevention of Cruelty to Animals (ASPCA) Animal Poison Control Center (APCC)

- Phone number: (888) 426-4435
- 24 hours a day, 365 days a year
- Consultation fee may apply

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Question #3

Which of the following is safe to recommend/administer in companion animals?

Acetaminophen

Ibuprofen

Naproxen

None of the above

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Question #3

Which of the following is safe to recommend/administer in companion animals?

Acetaminophen

Ibuprofen

Naproxen

None of the above

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Resources

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Pet Insurance

PAYS FOR VET COSTS

Plans typically pay-out for Veterinary treatment & medications, as well as some associated costs

COST

Typically costs less than the annual cost of food for your pet, between:

$200 to $500

BEST FOR YOUNG PETS

Policies will not pay for treatment of pre-existing conditions & cost less for younger animals

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Retail Savings Program for Pet Prescriptions

Walgreens Prescription Savings Club

- Family Option
  - $35/year (includes up to 5 family members - and pets
- Discounts on over 8,000 medications—no insurance necessary

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Pet Pharmacies

- Most pet prescriptions can be filled at retail pharmacies
- Internet pharmacies that fill pet prescriptions (i.e. Chewy, petco)

Add pet meds to cart and enter pet and vet info at checkout

Pharmacy contacts vet and verifies prescription

Meds delivered 1-3 vet after vet approval received

Weisbaum H. Pet insurance: How to get the best price and coverage. NBC News.

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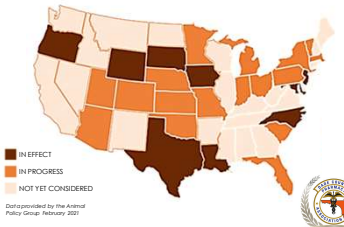
Drug References for Pharmacies

- Many state boards of pharmacy have amended their reference library requirements to require the inclusion of a veterinary drug reference
- This ensures safety and accuracy when dispensing medications for animals and counseling pet owners



Data provided by the Animal Policy Group February 2021

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FDA Green Book

- Animal Drugs @ FDA
  - Searchable online database; includes most FDA-approved and conditionally approved animal drugs

Search	Supporting Documents	Medicated Feeds and Veterinary Feed Directive

• Drug's proprietary name
• Active ingredient
• Application number
	• Environmental Documents
	• FOIA Drug Summaries
	  • Safety and effectiveness information submitted by the drug company to FDA to support the drug's
	• NSAID Labels
	• Blue Bird Labels
	  • Guides for manufacturers of medicated feed for how to prepare the final printed labels
		• Lists of feed mills that licensed to manufacture certain categories of medicated feed for food-producing animals
		• Lists of distributors that distribute animal feed containing a veterinary feed directive (VFD) drug

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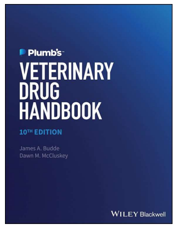
Plumb's Veterinary Drug Handbook

- Comprehensive and detailed source of drug information relevant to veterinary medicine
- Includes dosages, drug interactions, adverse effects, and contraindications (~768 drug monographs)
- Exhaustive coverage of drugs used in the care of a wide variety of species, including dogs, cats, birds, small mammals, and farm animals
- Annual subscription (available as a physical handbook, online database, or app)



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Summary

Pharmacists can contribute to veterinary medicine by compounding medications, dispensing prescriptions, and counseling pet owners for optimal animal well-being

Veterinary pharmacy practice is subject to state and federal laws, including the Controlled Substances Act

Pharmacists provide a range of medications for animals and understanding species-specific differences, potential risks, and dosage discrepancies is crucial for effective treatment

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Veterinary Medicine:
What Pharmacists Need Know

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Simple and Clean: USP 797 and USP 800 Updates

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Miami Beach, FL 33140
Sunday, January 21st, 2024

Objectives

- Describe the latest USP 797 and USP 800 standards and guidelines for sterile and hazardous compounding
- Analyze the role of pharmacists in institutional adaptation of USP guidelines
- Develop effective implementation strategies to meet USP standards

Abbreviations

- USP: US Pharmacopeia – sets compounding quality standards
- CSP: Compounded Sterile Preparation
- BUD: Beyond Use Date
- SCA: Segregated Compounding Area
- CAI: Compounding Aseptic Isolator
- PEC: Primary Engineering Control
- NIOSH: National Institute for Occupational Safety & Health
- HD: Hazardous Drugs
- C-PEC: Containment Primary Engineering Control
- C-SEC: Containment Secondary Engineering Control
- ACPH: Air Changes Per Hour
- RABS: Restricted Access Barrier System
- CACI: Compounding Aseptic Containment Isolator
- IWC: Inches of Water Column
- SOPs: Standard Operating Procedures

Why it Matters

Background: USP 797 and 800

- USP 797: Sterile Compounding
  - Sterile = products for sterile sites (IV, eyes, injections, inhalations)
  - Organizational policy and procedure compliance guidelines
  - Covers personnel training, equipment maintenance, product storage, and product sterility
- USP 800: Hazardous Drugs
  - Covers all handling of HD
  - Goal is to minimize exposure to toxic substances
  - Include sterile and non-sterile HD manipulation

USP General chapter <797>, <800> 2023

Background: USP 797 and 800

- USP 797 and USP 800 are live as of November 2023
- Does this mean they are enforceable?
- Joint Commission Statement: Can begin evaluating compliance with the revised chapters starting January 2024, unless state law allows for an extension
  - State of Florida Board of Pharmacy has granted an extension until 2025
- Florida Board of Pharmacy will not take disciplinary action for failure of compliance until November 2025

USP 797 Updates

Standard Operating Procedures

- New requirement: "Designated individual responsible and accountable for performance and operation of facility and personnel in CSP preparation."
- Facility must have standard operating procedures (SOPs) that include
  - Training, competency, assigned role and tasks for CSP preparers
  - Guidance to avoid contamination and error
  - System for recalling CSPs that are out of specified parameters

USP General chapter <797> 2023

Record Requirement

- Master Formulation Record (MFR)
  - Need for all CSPs made for > 1 patient or made with nonsterile ingredients
  - Preparation abides by evidence-based information (drug label, compatibility/stability studies)
  - "How we make the product"
- Compounding Records (CR)
  - Need for all CSPs including immediate use CSPs when made for > 1 patient (in bulk/batch)
  - "Record of what we made"

TABLE 1
Master Formulation Record Requirements

Name, strength or activity, and dosage form of the CSP/CNSP
Identities and amounts of all ingredients/components and for CNSPs relevant characteristics if applicable
BUD and storage requirements
Physical description of the final CSP/CNSP
Container closure system for all products and for CSPs the size of container closure system is also included
Reference source for stability (current <795> only indicates when available)
Quality control procedures (CNSP and results)
Complete instructions for preparing the CSP, including equipment, supplies, a description of the compounding steps, and for CSPs any special precautions (current <795> provides additional detail on order, duration, etc)
CNSPs mention labeling requirements (eg, shake well)
CNSPs require calculations if applicable to determine quantities and concentrations of APIs

Quiz

1. What do 797 standards operating protocols (SOPs) cover?
   A. Personnel training
   B. Equipment maintenance
   C. Product sterility
   D. All of the above

Quiz

1. What do 797 standards operating protocols (SOPs) cover?
   A. Personnel training
   B. Equipment maintenance
   C. Product sterility
   D. All of the above

CSPs – New Classification

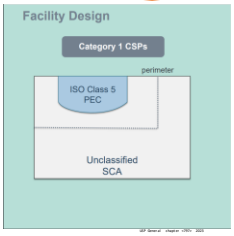
Low, medium, and high risk replaced by category 1, 2, and 3

2008 Requirements	2023 Requirements		
Risk-based:	Conditions-based: environment, starting ingredients, aseptic processing vs terminal sterilization, sterility testing, personnel garbing		
Low-risk with 12hr BUD	Category 1	Category 2	Category 3
Low Risk	• ISO 5 PEC • Unclassified SCA • Sterile ingredients • No additional testing	• Cleanroom suite • Sterile or nonsterile ingredients • Aseptic processing	• Cleanroom suite • Sterile or nonsterile ingredients • Additional garbing, cleaning and EM req's
Medium Risk			
High Risk			

Longer BUDs allowed when sterility testing and/or terminal sterilization performed

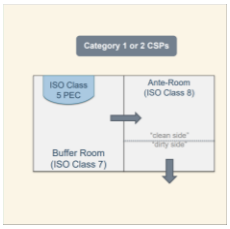
CSPs – Category 1

- Products made in areas that do not meet ISO 7 criteria
  - Segregated compounding areas
- Prepared in ISO 5 Primary Engineering Control (PEC)
- BUD depends on storage and drug stability
  - 12 hours room temperature (MAX)
  - 24 hours refrigerated (MAX)



CSPs – Category 2

- Include products made with:
  - ISO 5 PEC AND
  - Cleanroom suite ISO Class 7
  - Sterile or nonsterile ingredients
- BUD depends on
  - Storage
  - Ingredient sterility
  - Sterility testing
  - Aseptic technique and terminal sterilization where applicable
- Max BUD of 45 days (Room temp)



CSPs – Category 2

Preparation Characteristics		Storage Conditions		
Sterilization Method	Sterility Testing Performed and Passed	Controlled Room Temperature (20°-25°)	Refrigerator (2°-8°)	Freezer (-25° to -10°)
Aseptically Prepared CSPs	No	Prepared from one or more nonsterile starting component(s): 1 day	Prepared from one or more nonsterile starting component(s): 4 days	Prepared from one or more nonsterile starting component(s): 45 days
		Prepared from only sterile starting component(s): 4 days	Prepared from only sterile starting component(s): 9 days	Prepared from only sterile starting component(s): 45 days
	Yes	30 days	45 days	60 days
Terminally Sterilized CSPs	No	14 days	28 days	45 days
	Yes	45 days	60 days	90 days

CSPs – Category 3

- Can include complex production:
  - Non-sterile ingredients or devices
  - Stability concerns
- Category 3 CSPs:
  - **Require sterility testing**
  - Extended BUD calls for "environmental monitoring, sterile garb, sporicidal disinfectants, stability testing, and personnel qualification"
    - BUD max of 180 days
- Facility must meet Category 3 compounding requirements AT LEAST 30 days before Category 3 CSPS can be made.

Compounding Method	Controlled Room Temperature (20°–25°)	Refrigerator (2°–8°)	Freezer (−25° to −10°)
Aseptically processed, sterility tested, and passing all applicable tests for Category 3 CSPs	60 days	90 days	120 days
Terminally Sterilized, sterility tested, and passing all applicable tests for Category 3 CSPs	90 days	120 days	180 days

CSPs – More on New Category 3

- Compared to Cat. 2
  - Additional requirements can extend BUD
- Example of BUD if pass testing:
  - 60 to 90 days at room temp
  - 90 to 120 days refrigerated

Factors	Requirements	Criteria	
Ingredients	Components	Sterile or nonsterile starting ingredients	
Equipment	Pre-sterilization procedures	Weighing and mixing of nonsterile components must be completed in ISO 8 or better environment in a containment device or PEC	
Environment	Engineering Controls	ISO 5 PEC in and ISO 7 buffer room	
	Monitoring	Surface sampling weekly and with each batch. Must begin before assigning Category 3 BUDs	Air sampling monthly. Must be completed within 30 days prior to beginning Category 3
	Cleaning	Weekly sporicidal application	
Personnel	PPE	Sterile garb (no garb reused); no skin exposure in buffer room	
	Training	Gloving and Aseptic Validation	
CSP	CSP Testing – one time	Stability-indicating method study Particulate matter Container-closure-integrity test	
	CSP Testing – each batch	Sterility test – USP <71> Endotoxin test – USP <85>	
	Batch size	Maximum 250 units	

Garbing and Aseptic Responsibilities

- Language now requires "Anyone entering the sterile compounding area" to meet all personal hygiene and garbing
  - Not just sterile compounders
- Changes:
  - No longer allow hand dryers
  - Can't refill disposable soap containers, must be replaced
  - Facility can determine whether handwashing or garbing should occur first (include in SOPs)
  - Stricter policies on reusing garb:
    - Category 1 and 2 CSP – gown must be maintained in a manner than prevents contamination around or within compounding environment
    - Category 3 – Not allowed without laundering and re-sterilization

Garbing and Aseptic Responsibilities

- Initial competency requires 3 separate and consecutive successful garbing tests
- Media fill and gloved fingertip and thumb (GFT) sampling standards
  - GFT: Incubate at 30-35°C for at least 48 hours followed by incubating at 20-25°C for another 5 days (**minimum 7 days**)
  - Media fill: Incubate at 30-35°C for at least 7 days and at 20-25°C for at least 7 days (**minimum 14 days**)

	2008 USP 797	2023 USP 797
Action level for GFT	> 0 CFU	After garbing: > 0 CFU After media-fill: > 3 CFU (both hands total)

Training Frequency

Requirement	2008 Guidelines	Updated 2023 Guidelines
Training	• Yearly • Only those who prepared "high risk" CSPs needed to be assessed twice a year	• **At baseline, then** • **Every 6 to 12 months**

Garbing Competency	• Low / Medium risk
	  • Yearly
	• High risk
	  • Twice a year
		• **Category 1 and 2**
		  • **Every 6 months**
		• **Category 3**
		  • **Every 3 months**
		• **Personnel with direct oversight of compounders**
		  • **Every 12 months**

Aseptic Technique	• Low / Medium risk
	  • Yearly
	• High risk
	  • Twice a year	

- Formerly based on level of "risk"
- Now based on "category" of CSP

Quiz

2. How often must total particle counts for Category 1 and 2 CSPs be taken under USP 797?

A. Every 2 years
B. Annually
C. Every 6 months
D. Every 3 months

Quiz

2. How often must total particle counts for Category 1 and 2 CSPs be taken under USP 797?

A. Every 2 years
B. Annually
C. Every 6 months
D. Every 3 months

Nothing to Sneeze at: Specific Cases

- Allergenic extract compounding: USP 797 now addresses personnel training and competency for those who compound allergenic extract sets for prescription
- Requirements:
  - Baseline and yearly training
  - Pass 3 baseline and yearly fingertip tests
  - Yearly sterile technique evaluation

ACAAI Mixing Allergen Extracts 2023

- 6 months without compounding → re-evaluate core competencies

Facility and Labeling Requirements

- New cleanroom language
  - Relative humidity requirement of 60% or lower
  - ISO Class 8 room needs > 20 ACPH
  - Labeling must specify preparation is compounded
- Cleaning supplies must be
  - Low lint
  - Preferably disposable
  - Reusable supplies must be maintained within the area/SCA and cleanable non-porous material
  - STERILE (including water used for dilution)

Facility Testing Requirements

- Viable air sampling:
  - Must incubate for at least 48 hours at 30-35°C AND
  - At least 5 days at 20-25°C
- Surface sampling:
  - PEC staging/work area
  - Equipment in PEC
  - Frequently touched surfaces

	ISO Class 5	ISO Class 7	ISO Class 8
Action Level	> 3 CFU	> 5 CFU	> 50 CFU

Facility Assessment Frequency

Requirement	Category 1 & 2	Category 3
Surface sampling	Every month	• Every time an extended BUD is used • PEC surface at the end of each category 3 CSP batch before cleaning • Every week
Viable air sampling	Every 6 months	• 30 days before compounding can start • Every month
Total particle count	Every 6 months	Every month

What's the Beyond Use?

	Topical ophthalmic CSPs	Single-dose containers	Multi-dose CSPs	Single-dose and stock solution CSPs
Max beyond use date	Once opened: • 24 hours (room temp) • 72 hours (fridge)	12 hours or BUD	28 days or BUD	12 hours or BUD
Requirements	• Category 2 or 3 • For single patient • Label states temperature BUD terms	Punctured in ISO 5 or cleaner air	• Stored in BUD conditions (ex: fridge) • Meet antimicrobial testing and sterility requirements	• Punctured in ISO 5 or cleaner air • Stored in BUD conditions

Immediate Use Changes

- USP updates now allow items compounded for immediate use a maximum BUD of 4 hours
  - Previous USP 2008 allowed up to 1 hour only
- Update also removes many of the restrictions on immediate use compounding
  - No restriction on category of drug (risk level)
  - Allows for batching
  - No restrictions on "pokes" or compounding complexity other than max of 3 different sterile products allowed in preparation process

Immediate Use Changes

- Does this include nursing at bedside?

Compounding	Not Compounding
• Medication added to IV bag from vial • Medication prepared for future procedural use	• "Immediate administration" • Vial commercially prepared to be easily added to bag and activated • Preparation of alteplase in the ED • Medication drawn from vial into syringe for immediate dosage

- If preparing immediate-use CSP > 1 patient, must record in compounding record

Foreshadowing

- 2008 USP 797 guidelines allowed "a low volume of hazardous drugs" to be compounded outside of negative pressure
- 2008 USP 797 immediate-use guidelines do not allow for "immediate-use" compounding of antineoplastics
- New 797 guidelines do not have these restrictions
- What does the new USP 800 guidelines say?

USP 800 Updates

USP 800 – New Requirements

- Establishes separate USP 825 for Radiopharmaceuticals as CSPs
- New HD item list requirement
- Requires facility risk assessment
- Standard Operating Procedures (SOPs) must cover the following requirements
  - Designated areas for receiving, compounding, and handling HD
  - Surveillance and reporting
  - Personnel training and PPE standards
  - Decontamination, cleaning, and spill control

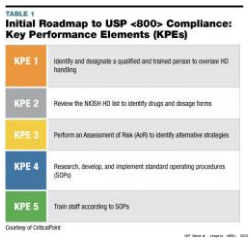


TABLE 1
Initial Roadmap to USP <800> Compliance: Key Performance Elements (KPEs)

KPE 1	Identify and designate a qualified and trained person to oversee HD handling
KPE 2	Review the NIOSH HD list to identify drugs and dosage forms
KPE 3	Perform an Assessment of Risk (AoR) to identify alternative strategies
KPE 4	Research, develop, and implement standard operating procedures (SOPs)
KPE 5	Train staff according to SOPs

Courtesy of CriticalPoint

Definition of a Hazardous Drug

- Hazardous drug:
  - Carcinogens
  - Teratogens
  - Reproductive toxicity
  - Organ toxicity at low doses
  - Genotoxicity
  - Structure/toxicity mimics existing HD
- Examples:
  - Cyclophosphamide
  - Methotrexate
  - Irinotecan
  - Warfarin
  - Azathioprine
  - Estradiol
  - Finasteride
  - Tamoxifen

USP 800 – New Requirements

- SOPs requirements must be available as WRITTEN protocols
  - Any receiving, compounding, or handling HD requires PPE standards
  - Surveillance should follow OSHA standards
  - Personnel training and PPE standards
    - Gown, gloves, shoe cover, head cover, eye, and respiratory protection
- Decontamination, cleaning, and spill control
  - Protocols for labeling, transport, and HD disposal should include training on exposure prevention, and how to use skill kits
  - Spill kits must be available in all HD areas
  - SOPs must document responsibility for spill management, required PPE, location of kits, and emergency clean up

USP 800: SOPs

- SOPs must cover
  1. Deactivation
     - EPA oxidizers – peroxide, sodium hypochlorite
  2. Decontamination
     - Remove residue – alcohol, water, peroxide
  3. Cleaning
     - Remove organic/inorganic material – germicidal agent
  4. Disinfection
     - Destroys microbes – EPA disinfectant or alcohol

NEW NIOSH and HD List Criteria

- Institution must implement and maintain a list of HDs used at facility
  - Must be reviewed every 12 months
  - Identification is required for any new HDs


Trade name: Propylthiouracil

Acute Toxicity - Oral 4 — H302 Harmful if swallowed

Label elements
GHS label elements
The substance is classified and labeled according to the Globally Harmonized System (GHS).
Hazard pictograms

GHS07 GHS08

Signal word Danger
Hazard statements
H302 Harmful if swallowed
H351 Suspected of causing cancer
H361 Suspected of damaging fertility or the unborn child.
H372 Causes damage to organs through prolonged or repeated exposure.

- An FDA approved drug is hazardous IF
  - Meets previously listed NIOSH criteria

  OR
  - Approved labeling has manufacturer's special handling information
- Change from 3 "groups" to 2 "tables"
  - No longer have separate reproductive toxicity group

OLD NIOSH List Criteria

3 categories/groups:

1. Antineoplastics
2. Non-antineoplastic that are elsewise hazardous
3. Reproductive risk

Examples

- Group 1: Methotrexate, irinotecan
- Group 2: Warfarin, azathioprine
- Group 3: Tretinoin, finasteride

New NIOSH HD Drug List Categories

Table 1:

- "Known human carcinogen" or "probably carcinogenic to humans"
- As identified by National Toxicology Program (NTP) or International Agency for Research on Cancer (IARC)

Table 2:

- Meets NIOSH HD criteria BUT
- Is not considered to be carcinogenic

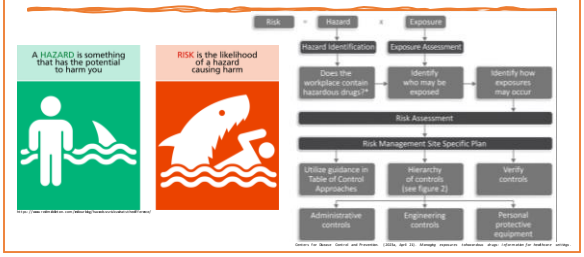
Both tables contain drugs that have known/suspected reproductive toxicity

	Table 1	Table 2
Examples	Azathioprine Cyclophosphamide Progesterone Propylthiouracil	Finasteride Methimazole Mycophenolate Nilotinib
Rationale	Listed by NTP or IARC as "known" or "probable" carcinogen	Not on NTP or IARC carcinogen lists

USP 800 – New Requirements

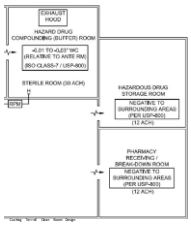
- Risk assessments
  - Every HD needs to be evaluated for exposure risk relative to dosage, packaging, and manipulation
  - Exposure risk must be assessed for every step of HD receiving, transport, compounding, dispensing, administration, and handling of spills and waste
  - Areas for HD handling must be clearly marked with signage

USP 800 – Risk Assessment



USP 800: A Lot to Unpack

- HD must be unpacked in negative or neutral pressure areas only
- Store to prevent spills/breaking
- Store away from nonhazardous drugs
  - Exceptions that can be stored with non-HD meds:
    - Non-antineoplastic HDs that are reproductive risk only
    - Final dosage forms of antineoplastics
- Antineoplastic HD storage must be externally ventilated, under negative pressure, and have 12 air changes per hour



Wake-up! Pop Quiz

- Is misoprostol a hazardous drug?
  - What category/group?
- Can misoprostol oral tablets be stored in a med carousel with nonhazardous drugs?

USP 800: Under Pressure

- HD compounding areas must be negative pressure, with fail-safe ventilation power sources in case of power loss
- C-PECs including vertical flow hoods, must be in C-SECs that are externally ventilated
- USP 800 allows for compounding in Containment-Segregated Compounding Areas (C-SCAs)
  - BUD 12 hours at room temperature or 24 hours refrigerated MAX
- C-SCAs and any HD compounding area
  - Need **negative pressure** -0.01 to -0.03 iwc
  - Need ≥ 12 air changes per hour

USP 800: Under Pressure

- PPE: HD gown, head/shoe cover, 2 pairs of chemotherapy gloves
  - Gloves must be changed every 30 minutes (or if torn/contaminated)
- Personnel must be re-evaluated for competency every 12 months
  - New training for new HDs, new equipment, workflow changes
  - Documentation of competency must be kept while person is employed on site

Quiz

3. True or False: Under USP 800, hazardous drugs can only be unpacked in positive pressure rooms.

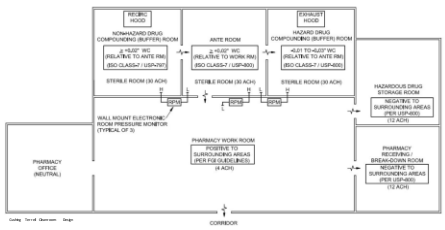
Quiz

3. True or **False**: Under USP 800, hazardous drugs can only be unpacked in positive pressure rooms.

Future

- Florida Board of Pharmacy 2025 extension
- Pharmacists bridge clinical practice to the physical and technological requirements of compounding
  - Facility, equipment, and space compliance
  - Training, cleaning, monitoring frequency
  - Beyond-use dating
- Feedback for USP:
  - USP Expert Committee meetings allow open attendance
  - USP website has links for feedback and questions

Looking for a New Apartment?



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Questions?

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