MEDICAL MARIJUANA: PHARMACOLOGIC CONSIDERATIONS AND REGULATORY UPDATE

Learning Objectives
- LIST the potential therapeutic applications of marijuana.
- DESCRIBE the pharmacology and pharmacokinetics of marijuana.
- DESCRIBE the differences and similarities among states in their oversight of marijuana used for medical and non-medical purposes and the pharmacist’s role.
- REVIEW the conflict between state and federal law as it applies to marijuana and the significance of recent changes.

Post-test/Rationale:

1. The number of states which have NOT approved any type or form of marijuana for medical use is:
   A. 0
   B. 3
   C. 17
   D. 30

   Answer Rationale: Only 3 states (as of November 2018) prohibit the use of any marijuana product for medical use (Idaho, Kansas, and Nebraska).

2. A cannabinoid found in marijuana with has potential for medical use, but which does not have psychoactive properties is:
   A. Delta-9-THC
   B. Delta-11-THC
   C. Cannabidiol
   D. Anandamide

   Answer Rationale: The 2 most abundant and well-known cannabinoids are delta-9-tetrahydrocannabinol (delta-9-THC), which, along with the closely related but less potent delta-8-tetrahydrocannabinol (delta-8-THC), are believed to be the principal psychoactive compounds found in the plant, and the non-psychoactive cannabidiol (CBD).

3. Which statement about the medical use of marijuana is incorrect?
   A. Cannabinoids act on CB receptors but their clinical activity may be due to other mechanisms
   B. There are many large, controlled clinical trials consistently demonstrating efficacy of marijuana
   C. Pharmaceutical manufacturers are developing synthetic drugs targeting cannabinoid signaling.
   D. Smoked marijuana has a faster onset of action than oral

   Answer Rationale: While numerous individual reports describe promising activity, meta-analyses of most of the published research studies have shown variable, inconsistent, and conflicting results and modest to weak effects on a number of disease states; conclusions are also hindered by short term investigations, small sample sizes, and subjective effects
4. The National Academy of Sciences concluded that there is substantial evidence that marijuana is useful in treating:
A. Pain***
B. Glaucoma
C. Depression
D. Dementia

Answer Rationale: The therapeutic conclusions reached by the Committee are shown in Table 1. The strongest evidence in the Committee’s view was in reducing chemotherapy-associated nausea and vomiting, treating pain, and relieving subjective spasticity associated with multiple sclerosis.

5. Which of the following is NOT a side effect of medical marijuana?
A. Drowsiness
B. Difficulty in concentration
C. Dry mouth
D. Bradycardia***

Answer Rationale: Some reported adverse effects of marijuana include decreased short-term memory; impaired motor skills and driving abilities; dry mouth; tachycardia, palpitations, hypertension and other adverse cardiovascular events; reduced immunologic competence; bronchitis (when smoked); and depression, psychotic behavior and altered cognitive function with high dose chronic use.

6. The primary enzymes which metabolize THC and CBD are:
A. CYP3A4 and CYP2C19***
B. CYP2C9 and CYP1A1
C. CYP2D6 and CYP1A2
D. CYP2E4 and CYP2C6

Answer Rationale: THC is predominantly metabolized by CYP3A4, CYP2C9, and CYP2C19 mainly to the active 11-hydroxy-THC and the inactive 11-carboxy-THC and is subsequently glucuronidated and excreted in the urine and feces. CBD is metabolized primarily by isozymes CYP3A4, CYP2C19, and to a lesser extent by CYP1A1, CYP1A2, CYP2C9, and CYP2D6. A general rule of thumb for pharmacists would be to monitor for common CYP2C9, CYP2C19, and CYP3A4 inhibitors and substrates since cannabinoids could affect clinical activity.

7. Cannabidiol (Epidiolex) has been approved by the FDA for treating:
A. Nausea and vomiting
B. Pediatric seizure disorders***
C. Glaucoma
D. Pain
Answer Rationale: In October 2018, the FDA approved an oral cannabidiol solution (GW Pharma’s Epidiolex) for the treatment of seizures associated with Lennox-Gastaut (LGS) and Dravet syndrome (severe myoclonic epilepsy of infancy) in patients 2 years of age and older.

8. Marijuana and its components are currently regulated by the DEA in what schedule?
   A. Schedule I***
   B. Schedule II
   D. Schedule I in most states, but Schedule II in states with a medical marijuana program
   D. They are not in any Schedule

Answer Rationale: Under the CSA, marijuana is a Schedule I Controlled Substance, meaning that it has a high potential for abuse and no currently accepted medical use. In fact, the DEA takes a broad view of what marijuana means, including all parts of the plant, the resin, and every compound found in the plant being subject to control.

9. Which of the following is correct with regard to Pharmacist oversight of medical marijuana?
   A. All states require pharmacist oversight of dispensing
   B. No state requires pharmacist oversight of dispensing
   C. In at least one state, only a pharmacist may dispense medical marijuana***
   D. Retail pharmacists are required to inquire about marijuana use when counseling a patient

Answer Rationale: The most pharmacist involvement is in Connecticut. In Connecticut, a marijuana dispensary must be licensed by the Department of Consumer Protection (the agency responsible for regulating pharmacies in this state) and the number of dispensaries is restricted (currently 9 for the entire state). In addition, only a licensed pharmacist in good standing can dispense marijuana. Pharmacists are also required to enter information regarding the dispensing of marijuana into the state’s prescription monitoring program database (as is required for all controlled substances).

10. What change in scheduling did the DEA recently implement?
    A. They rescheduled all cannabidiol products as C-I
    B. They rescheduled all cannabidiol products as C-V
    C. They endorsed rescheduling marijuana as C-II
    D. They rescheduled a single FDA-approved form of cannabidiol as C-V***

Answer Rationale: CBD now belongs in a special category; FDA approval of Epidiolex required rescheduling. Since the U.S. is a signatory to the “Single Convention,” a 1961 international treaty designed to control trafficking in controlled substances, the Justice Department was required to place appropriate controls on CBD as a listed substance in the treaty. Previously, all forms of cannabidiol were C-I under the CSA. The DEA acknowledged that “Epidiolex no longer meets the criteria for placement in schedule I of the CSA” since it received FDA approval and can no longer be considered to have no medical use. The DEA could have placed the drug in Schedule II, but elected, with advice from the FDA, to designate it as a Schedule V drug instead.50