

Minnesota Poison Control System Treatment Guideline:

Cannabis (marijuana)

Pharmacology & Summary in Overdose/Poisoning:

Pharmacology

Cannabis is the most commonly consumed drug in the world,¹ and is generally well-tolerated.² As of 2022, it has also been approved for medicinal use by qualifying patients in 39 states and the District of Columbia, and is available for adult recreational use in 19 states. Though there are hundreds of chemical components in marijuana (including cannabinoids, terpenes, lipids, flavonoids, etc), the most commonly referenced and typically most plentiful substance is the psychoactive cannabinoid Δ^9 -tetrahydrocannabinol (Δ^9 -THC, also known simply as THC). Non-psychoactive cannabinoids, such as cannabidiol (CBD, a substance recently employed for use in the treatment of Dravet syndrome and Lennox-Gastaut syndrome), are also present in marijuana. Products colloquially referred to as “marijuana” are derived from the *Cannabis sativa* plant.

Cannabinoids bind CB receptors, of which there are two types (CB₁ located primarily in the brain, and CB₂ located in immune cells). CB receptors are found in differing concentrations throughout the body’s organs and tissues. CB receptors have endogenous ligands, known as endocannabinoids (e.g., anandamide, and 2-arachidonoylglycerol [2-AG]), and together are known as the endocannabinoid system (ECS). Endocannabinoids are synthesized “on demand” and work as “retrograde messengers” and travel backwards to regulate the release of neurotransmitters; this results in decreased release of both inhibitory and excitatory neurotransmitters with the net effect functioning to regulate as a “rheostatic” regulator on neuronal excitability.

Δ^9 -THC is nearly completely metabolized by hepatic hydroxylation and oxidation (CYP2C9 and CYP3A4). The primary metabolite is 11-hydroxy- Δ^9 -tetrahydrocannabinol (11-OH- Δ^9 -THC), which is active and likely more potent than THC. 11-OH- Δ^9 -THC is subsequently metabolized via CYP2C9 to the inactive 11-nor- Δ^9 -THC carboxylic acid (THC-COOH). THC to 11-OH-THC conversion is generally higher when taken orally versus when smoked.

Synthetic cannabinoid receptor agonists (SCRAs; “K2,” “Spice,” etc.) also produce effects via interactions with CB₁ and CB₂ receptors, but have unique clinical effects³ and are outside the scope of this guideline.

Dosing & Clinical Effects

Several dosage formulations exist for Cannabis products, but most can generally be categorized into 3 main delivery groups: products for inhalation, oral ingestion, and topical use. THC is 10-35% bioavailable when smoked, with effects occurring within minutes² with intoxication lasting up to 4 hours. Two to 3 mg of inhaled THC⁴ may be intoxicating in naïve adult users. THC taken orally is 5-20% bioavailable with a peak



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effect at 1 - 3 hours,⁵ as little as 5 mg⁴ may be intoxicating for a naïve adult user with effects lasting 12-24 hours.

Clinical manifestations vary based on age. In adults, Cannabis overall carries low risk for severe toxicity. Inebriating effects leading to poor judgment and concomitant use of other medications may lead to increased risk of falls or other injuries. In contrast, severe toxic effects of cannabis ingestions have been seen at doses at 5-300 mg in children,⁴ and have been increasing,⁶ particularly in U.S. states where decriminalization⁷ and legalization⁸ occur.^{9,10} In *small children*, neurologic effects, including ataxia, hyperkinesia, lethargy, may occur; however, *coma and respiratory depression are the greatest concern*¹¹ and can occur even with small accidental ingestions.^{12,13} Seizures may also occur.¹⁴ Nausea and vomiting are also common.¹⁴ Cardiovascular symptoms may include bradycardia and hypotension.¹⁴ Severity of symptoms are dose-dependent, and more severe at lower doses in Cannabis-naïve children.¹³ In a small series of 38 children from a pediatric emergency department, 3.2 mg/kg of THC led to observation and minimal interventions, 7.2 mg/kg led to inpatient admission and moderate interventions, and 13 mg/kg led to ICU admission and major interventions.¹³

In adults, acute intoxication is more varied than in children. Neurologic symptoms may include dysphoria, slurred speech, ataxia, agitation, and delirium. Psychosis may also occur, and may persist long after acute intoxication would be expected to resolve. Nausea and vomiting are common in acute intoxication, particularly with oral ingestions. In contrast to children, tachycardia and hypertension are more common in adults.¹ Cardiac complications such as dysrhythmias¹⁵ and acute myocardial infarction¹⁶ are associated with Cannabis use but are rare. Chronic, heavy marijuana use is associated with a clinical syndrome of abdominal discomfort, nausea, and cannabinoid hyperemesis syndrome (CHS).¹⁷ CHS has become more common with the legalization and commercialization of Cannabis.^{18,19}

Common dosing information for THC

- Starting doses of ingested THC for an adult is typically 1 - 10mg.
- Gummies/edibles are commonly available as 2 - 10 mg THC per piece, but can range as high as 60-80 mg per piece in some states.
 - In the state of Minnesota as of July 2022, THC edibles are limited to 5 mg per serving and 50 mg per package.²⁰
- The average joint will contain 15-30 mg THC to start (depends on strain and concentration of flower product used; actual content subject to pyrolysis).



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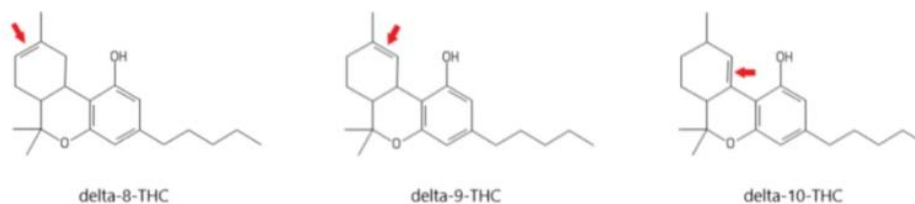
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Clinical Effects of Cannabinoids other than $\Delta 9$ -THC

CBD products – Cannabidiol or CBD products have gained much attention over the past several years, as their use and efficacy in refractory seizure disorders has been evaluated and found effective in clinical trials. The only commercially available CBD-only product that has been deemed to be “THC-free” is the prescription product “Epidiolex (which FDA approved for treatment of Dravet Syndrome and Lennox Gastaut syndrome).²¹

CBD is generally considered to be not psychoactive, however over-the-counter products sometimes contain impurities and other psychoactive compounds, including psychoactive cannabinoids.²²

$\Delta 8$ -THC products – Recently, there has been an increased availability of products claiming to contain the “less-potent” cannabinoid, $\Delta 8$ -THC. $\Delta 8$ -THC is chemically identical to $\Delta 9$ -THC with the exception of a single carbon double-bond²³ (see figures).



$\Delta 8$ -THC binds cannabinoid receptors in a similar fashion to $\Delta 9$ -THC, but are purported to have less potent effects on a mg-to-mg basis. To date, an exact potency comparison is not known, but it has been suggested online that $\Delta 8$ -THC is approximately half as potent in overall effects including psychoactivity as those of $\Delta 9$ THC.²³ The safety of $\Delta 8$ -THC in children, in particular, has a very poor evidence base.^{24,25} Currently, $\Delta 8$ -THC products are being sold through a purported legal loophole in the language of the 2018 “Farm Bill” (the Agriculture Improvement Act of 2018, which amends the definition of “Marihuana” is limited to extracts of Cannabis sativa “containing greater than 0.3 percent delta-9-tetrahydrocannabinol on a dry weight basis”).²⁶ After passage of the 2018 Farm Bill, manufacturing of $\Delta 8$ -THC by chemically modifying CBD became more common, and $\Delta 8$ -THC products became more widely available. The legality of these products is currently being litigated.^{27,28} Unlike CBD, users of $\Delta 8$ -THC likely will have positive urine immunoassays for “THC” because of the similarity in chemical structures.²³ Recently, $\Delta 10$ -THC products have been sold for similar purposes (see figure above); the potency and toxicity of $\Delta 10$ -THC²⁹ is less certain than that of $\Delta 8$ -THC.

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For Δ8-THC, Δ9-THC, and/or Δ10-THC, the following may be observed at home:

Children

- Lick, drop, or taste amounts & unwitnessed ingestions as long as patient is:
 - Asymptomatic
 - Parent/caregiver is available and responsible
 - Transport to hospital or access to 911 is readily available
 - See exceptions below regarding imminent expected sleep (e.g., naps, bedtime)
- Children treated with CBD oil, Epidiolex, or other CBD-only products for seizures who received an extra or increased dose of their product, and are asymptomatic.

Adults

- Most adult cases may be followed at home if the patient has mild to moderate symptoms such as somnolence, alterations in sense and time perception, depersonalization, and mood alterations.
 - Home monitoring in such patients is reasonable if the patient is able to drink fluids/maintain normal hydration

Recommendations for Home Care

- Monitor the patient (allowing for rest) in an area with minimal stimuli

Guidelines for Follow-up:

- Callers should be instructed to immediately call the poison center if the patient develops any cardiac symptoms (e.g. dyspnea, chest pain), any evidence of respiratory depression, or if neurologic status worsens.
- A follow-up call should be made 1 hour post-exposure in children, and 2-3 hours post-exposure in adults
 - Children monitored at home should receive a follow-up call once per hour until 3 hours post-exposure
 - Follow-up beyond 3 hours is at the discretion of the SPI
 - If the patient is asymptomatic *at 3 hours*, no further follow-up is required
 - If vomiting is present, cases should be followed until vomiting has stopped and the patient is able to drink fluids.



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The following should be referred to a health care facility:

- Weight-based triage thresholds by age (for $\Delta 8$ -THC, $\Delta 9$ -THC, and/or $\Delta 10$ -THC):³⁰
 - 6 months - 5 years: > 0.2 mg/kg
 - 6 years - 12 years: > 0.3 mg/kg
 - 13 years - 79 years: > 0.4 mg/kg
- All children who are drowsy, regardless of dose ingested
- All children, regardless of dose ingested or symptoms, expected to sleep in the next 3 hours (i.e., those with exposures within 3 hours of their usual nap or bedtime).
- Patients with significant mental status changes, including confusion, obtundation or coma.
- Patients ingesting concentrated products meant for use by other delivery modes (e.g., oils, butters, shatters)
- Patients with persistent vomiting that are unable to drink fluids
- Patients deemed at risk for intentional-self harm (e.g., possible suicide attempts)

Treatment:

- Supportive care is the mainstay.
- A period of 3-4 hours of monitoring for asymptomatic children will typically facilitate safe discharge home.
- Treatments for acute vomiting in CHS:
 - The optimal antiemetics are likely antipsychotics.
 - Droperidol seems to be particularly effective.³¹
 - Some patients report relief with warm showers
 - Capsaicin cream (0.025% - 0.1%), applied to the abdomen, has been successfully used.^{32,33} Some patients find this uncomfortable.
- Benzodiazepines are recommended for agitation, hallucinations, or seizures.

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