EDUCATIONAL GUIDE

KRATOM

A brief educational guide for clinicians about what Kratom is, why and how it is used, and clinical management.





Kratom 101	1
Legality	3
Clinical Management	4
Specific Population Considerations	7
References	8

KRATOM 101

WHAT IS KRATOM

Kratom is a tropical evergreen tree native to Southeast Asia and in the U.S., most comes from Indonesia. It is a traditional folk medicine that has been used to treat several conditions for centuries, most notably musculoskeletal pain, anxiety, and depression. Kratom may be chewed, smoked, or transformed to powder that can be used as a tea or consumed as a capsule.¹

Kratom contains over 40 alkaloids. Its main active ingredients are mitragynine and 7-hydroxymitragynine.¹ The most prevalent is mitragynine. Depending on how much Kratom the person has consumed, the drug can have stimulant-like effects or opioid-like effects.

Prevalence of Kratom Use

Estimates of Kratom use vary widely:

- According to the National Survey on Drug Use and Health (2020), the estimated past-year rate is 0.8% (2.1 million).²
- Covvey et al. (2020) estimates 6.1% of the general population have tried
 Kratom.³
- The American Kratom Association estimates 15 million people use Kratom each year.

Kratom is NOT regulated by the FDA or scheduled by the DEA. It can be obtained from places like the internet, "legal high" shops, gas stations, smoke shops, and kava bars. Hot spots include Florida and California.

Why do people use Kratom

According to Garcia-Romeo et al. (2020), people report using Kratom for a variety of reasons such as:⁴

- Treat pain
- Treat opioid withdrawal symptoms
- Treat anxiety and depression
- Limit or discontinue opioid, other drug or alcohol use
- Boost concentration
- Experience euphoria

Overdose

In 2018, the FDA issued a warning that kratom has a similar structure to opioids and identified 44 deaths related to kratom use. For overdose deaths reported that identified Kratom, the majority of showed multidrug ingestion. It is important to note that because testing for Kratom requires special testing and often not completed, actual overdose rates are likely underestimated.

Considerations from Florida:

In 2020, Florida began requiring testing for Kratom as part of post-mortem toxicology. According to a review published in the Tampa Bay Times in 2023, medical examiners have identified 587 overdose deaths involving Kratom since 2013. 533 overdoses involved multi-substance overdoses involving Kratom and 46 Kratom-only overdoses.⁶

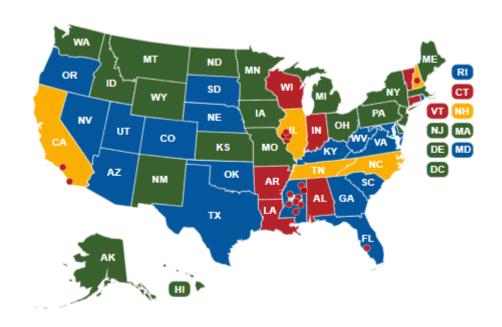
PRESCRIBE NALOXONE

Because Kratom is not regulated by the FDA and often contains other drugs, always prescribe naloxone to patients using Kratom. Although clinical effectiveness in reversing effects of Kratom has not been proven, there is a case report of successful resuscitation of opioid toxidrome attributed to sole Kratom use.⁷



IS KRATOM LEGAL?

The legality of Kratom varies by state. Some states have adopted the Kratom Consumer Protection Act which requires the FDA to hold a hearing and establish a task force to look at the safety of products containing Kratom. ⁸





GREEN = Kratom is legal in the state

ORANGE = States legal but with some known local bans or with exceptions.

RED DOT = Banned city

RED = Kratom is illegal and banned in the state

BLUE = State has adopted the Kratom Consumer Protection Act bill

There is no age limit to purchase Kratom in areas where it is not regulated.

CLINICAL MANAGEMENT

For patients dependent on Kratom, management of withdrawal and treatment is similar to opioid use disorder.

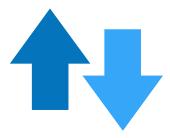
Pharmacodynamics

Kratom reaches peak concentration in approximately 2 hours. Its half-life varies greatly. Studies report a half-life of 3-24 hours.

Pharmacokinetics

Depending on how much Kratom the person has consumed, the drug can have stimulant-like effects or opioid-like effects.^{9,10}

When consumed in larger doses, Kratom has opioid-like effects



When consumed in smaller doses,
Kratom has stimulant-like effects

Stimulant-like at low doses < 5 g Opioid-like at 5-15 g Sedation at >15 g

Kratom acts as agonists at the mu-opioid receptor and antagonist at the kappa and delta opioid receptors in vitro. It has less affinity for opioid receptors than morphine. Because it has a broad affinity for receptors including serotonergic, adrenergic, and GABAergic pathways, Kratom can be linked to stimulant effects:

- Agonism of Alpha2 (possible Alpha1) receptors
- Agonism of 5-HT2A receptors (and 5-HT1A) receptors

Medication Interactions

Kratom inhibits multiple cytochrome P450 isoforms (CYP) including CYP2D6 and CYP3A. CYP3A4 is responsible for the metabolism of more than 50% of medicines. Potent inhibitors of CYP3A4 include: clarithromycin, erythromycin, diltiazem, ketoconazole, ritonavir, verapamil, and grapefruit. Many websites advise "potentiating" the Kratom experience with grapefruit juice. Inducers of CYP3A4 include phenobarbital, phenytoin, rifampicin, St. John's Wort and glucocorticoids.¹⁰

Adverse Effects

The most common experienced are:

- Agitation
- Tachycardia
- Nausea
- Vomiting
- Fatigue/drowsiness
- Hypertension
- Confusion
- Seizures are common



There have been cases of Kratom causing psychotic symptoms such as hallucinations and delusions.¹²

Testing for Kratom

Testing can be done for mitragynine which is one of the main active ingredients. However, it requires advanced tests like liquid chromatographytandem or mass spectrometry. It is unclear how long the drug is present in the urine but likely is dose dependent.¹³

Diagnosis

There is not an ICD-10 diagnosis for Kratom use disorder.

Currently, ICD-10 diagnosis code, F19. 99 "Other psychoactive substance use, unspecified with unspecified psychoactive substance-induced disorder" is the most applicable. Treating Kratom use disorder and subsequent withdrawal is similar to how opioid use disorder is managed.

Withdrawal

Withdrawal from Kratom is very similar to opioid withdrawal. ^{9,10} Signs and symptoms of withdrawal may include:

- Anxiety
- Irritability
- Cravings
- Restlessness
- Fatigue
- Insomnia
- Nausea

- Body aches
- Depressed mood
- Hot flashes
- Cold flashes
- Runny nose
- Watery eyes
- Vomiting

Treatment

Treating Kratom use disorder and subsequent withdrawal is similar to how opioid use disorder is managed. Medications like buprenorphine can be used to manage withdrawal and dependence.¹³ Dosing for buprenorphine is similar to opioid use disorder management. In our experience, most patients transitioning from Kratom to buprenorphine have significant anxiety requiring supportive alpha-2 agonists like clonidine. These symptoms are secondary to sympathetic overactivation.¹⁴

SPECIFIC POPULATION CONSIDERATIONS

Adolescents

Kratom use in adolescents is a concern due to:

- Wide availability
- · Ease of access
- No age restriction to purchase in places where it is not regulated

Information from the National Poison Data System shows that between the years of 2011 and 2017, 84.7% of adolescents that used Kratom were between the ages of 17 to 19 years old.¹⁵

Pregnant Persons

From a peer literature review conducted in 2021, there were five published case reports that met inclusion criteria. There were six pregnant persons included who used Kratom during pregnancy. All deliveries were full term.¹⁶

- Polysubstance use was reported in four out of six persons
- Treatment plans for the pregnant persons was similar to typical opioid treatment plans
 - All reported successfully weaning off of Kratom
- Five out of six infants experienced neonatal abstinence syndrome (NAS)
 including the two that were only exposed to Kratom
 - Additional research is needed to understand the timing of withdrawal compared to prenatal Kratom exposure

All pregnant persons should be screened using a validated tool for substance use and offered evidence-based treatments when necessary.

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