Some of my patients have mentioned using kratom (mitragynine) to help with opioid-withdrawal relief. Should I be concerned about its potential for abuse and, if so, what adverse events have been identified?

Although there is conflicting evidence on kratom’s abuse potential, several case reports have found a correlation between kratom use and physical dependence/addiction. Irritability, insomnia and myalgias have been observed after the discontinuation of kratom.1,2 Studies have documented nausea, tachycardia, seizures, liver toxicity and respiratory depression as side effects after use of kratom.3,4 Because of the need for more research, the Food and Drug Administration (FDA) and Centers for Disease Control and Prevention (CDC) currently discourage its use.

Kratom, botanically known as Mitragyna speciosa, refers to a tropical tree found in parts of Southeast Asia belonging to the Rubiaceae family.5,6 The leaves of this tree have traditionally been used as an herbal remedy in the treatment of fatigue, cough, diarrhea, and opioid withdrawal symptoms. Kratom has conventionally been self-administered by chewing fresh leaves or adding dry, crushed leaves into herbal teas and other drinks.5,6 Due to its desirable opioid-like and psychoactive effects, its use has gained popularity in the United States. Today, it is commonly marketed as a dietary supplement in capsule or tablet form easily accessible online and in specialty stores.7

Kratom produces both analgesic and stimulant effects due to the properties of its main active alkaloids: mitragynine and 7-hydroxymitragynine (7-HMG).8 Mitragynine produces opioid-like analgesic effects by acting as a µ-opioid receptor agonist. Stimulant activity is believed to be due to inhibitory activity on serotonergic 5-HT2A receptors and activation of postsynaptic alpha-2 adrenergic receptors.9,10 Mitragynine is renally excreted after undergoing biotransformation.1,8,11 7-HMG, although a minor component, seems to demonstrate much higher levels of antinociceptive, sedative, and stimulant potency.12,13

Kratom’s effects are dose-dependent in nature. Increased alertness, energy, talkativeness and social behavior along with other stimulant properties are seen at doses of 1-5 grams. Increasing doses to 5-15 grams can result in patients experiencing more opioid-like effects such as sedation, constipation, dizziness, hypotension, dry mouth and sweating. Beyond these doses, lethargy, dysphoria and euphoria are common.14 These effects can be seen as early as 10 minutes post-administration and usually last about 5-7 hours.14 Other common adverse effects include: anxiety, agitation, nausea, loss of appetite, tremor, insomnia, weight loss, hyperpigmentation, seizures and hallucinations.16 Drug-drug interactions are possible due to kratom’s potential to inhibit several major CYP450 enzymes (CYP1A2, 3A4, and 2D6).15

Kratom is currently being researched for use in alcohol and opioid withdrawal, infection, weight loss, control of chronic or acute pain, diarrhea, and as an adjunct to diabetes therapy.16,17 Currently, both the FDA and CDC have sided against recommending its use by acknowledging a lack of substantial evidence.18 The Drug Enforcement Agency (DEA) has placed it on the “Drugs and Chemicals of Concern” list due to safety concerns with its use.19 Kratom’s lack of regulation has led to reports of poor manufacturing practices and adulteration with the addition of the more potent alkaloid, 7-HMG, in several commercial kratom products.20

Additionally, kratom may be combined with other drugs to form illicit substances; one such example is krypton, which includes O-desmethyl-tramadol. An interpretive comment alerts the provider to the possibility of krypton when tramadol is not prescribed and O-desmethyl-tramadol is detected in absence of other tramadol markers.

Aegis now provides definitive testing for kratom (mitragynine) via liquid chromatography- tandem mass spectrometry (LC-MS/MS).
REFERENCES: