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First Script Prescription Benefit News
for Workers' Compensation

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I read recently about different supplements and investigational drugs that people are obtaining to help with opioid withdrawal. One was a product from Africa that is illegal in the U.S. Can you offer more information related to this substance?

Ibogaine is a psychedelic substance derived from the root bark of the western Central African rainforest shrub *Tabernanthe* iboga. It produces hallucinogenic effects similar to those associated with LSD and has been known to put users into a dream-like state. It has been used in various doses in Canada, Mexico, and Europe for management of withdrawal symptoms and reduction of cravings in patients with opioid addiction; however, the drug is illegal in the United States and is classified as a Schedule I Controlled Substance. A few states in the U.S. have introduced legislation to support pilot studies of ibogaine for such uses, including Maryland, New Hampshire, New York, and Vermont, but none have yet passed.

Clinical trials related to the potential of hallucinogens to minimize challenging medical effects is nothing new, although support for such practice is met with resistance, much skepticism, and is often considered a last resort. However, the research remains fascinating, and several institutions such as John Hopkins N.Y.U have begun to delve into the applications of drugs such as LSD and ibogaine for treatment-resistant patients suffering from depression and other mood disorders, PTSD, and smoking or opioid addiction with favorable success rates.

Interestingly, the American Addiction Centers (AAC) point out that when it comes to efficacy for addiction, the thought is that rather than managing withdrawal symptoms, ibogaine essentially interrupts the process. Because addiction is considered a disease of the brain where physiologic changes have occurred in the body's reward system, ibogaine, in theory, works to "rewire" the brain and targets those areas of the brain involved in drug-seeking and addictive behaviors, resetting them to the state prior to the drug addiction. Ibogaine's results touted by the AAC's website are a bit foggy, but they point to up to a 50% opioid abstinence rate after a one-year follow-up period. The AAC provides a comparison abstinence rate for Suboxone®, a buprenorphine and naloxone product FDA-approved for the maintenance treatment of opioid dependence, which is listed as an 8.6 percent success rate "once the person no longer needs to take Suboxone."[1]

Ibogaine and its active metabolite (noribogaine) interact with a number of neurotransmitters within the body, including dopamine, achetylcholine, serotonin, N-methyl-D-aspartate (NMDA) receptors, and kappa- and mu-opioid receptors. Of note, many of these chemicals substances and receptors play a role in the body's pain pathway and are affected by drugs we have on the market today to improve mood or alleviate pain. Dosing for ibogaine varies, but many studies appear to use a range of 10 to 25 mg/kg given as a single dose for opioid detoxification.[2-4] While ibogaine itself has a relatively short half-life of 4 to 7 hours, its primary active metabolite has a prolonged half-life of 28 to 49 hours.[2] This means that the drug can have sustained effects in the body as it takes several days to clear completely.

Drugs such as ibogaine are not without adverse effects. Ibogaine has been associated with cardiotoxicity and can prolong the QT interval which may lead to arrhythmias, including life-threatening Torsades de pointes (TdP). Death from cardiac complications has been reported in subjects taking ibogaine with and without underlying cardiovascular disease.[5] Of note, methadone, a long-acting opioid often used in detoxification today, also carries a risk of QT prolongation and TdP. Studies have suggested that ibogaine may be neurotoxic at high doses as well.[3]

Due to the illegal nature of the drug and the concerning potential for adverse effects, ibogaine should never be purchased online or self-administered. While ibogaine use for addiction is an interesting topic, supporting evidence remains limited and more research, including in-depth clinical study, is needed to fully evaluate the safety, efficacy, and potential of this drug.

References:
1. https://americanaddictioncenters.org/meth-treatment/success-rate-for-ibogaine/
2. https://www.sciencedirect.com/science/article/pii/S0099959801560125?via%3Dihub
3. https://www.ncbi.nlm.nih.gov/pubmed/18029124
4. https://www.ncbi.nlm.nih.gov/pubmed/10506904
5. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4382526/

Drug of the Month

Cassipa (buprenorphine and naloxone)

Cassipa (buprenorphine and naloxone) sublingual film was approved by the Food and Drug Administration (FDA) on September 7, 2018 for the maintenance treatment of opioid dependence. Cassipa is a Schedule III Controlled Substance containing the long-acting partial opioid agonist buprenorphine in combination with the opioid antagonist naloxone, similar to brand name Suboxone®. Like Suboxone, Cassipa's formulation is such that naloxone (the opioid antagonist component) is only active and will block and reverse the effects of the opioid if the sublingual film is tampered with for administration through a different route such as injection, for example, as might be attempted for abuse of the opioid ingredient.

Cassipa is intended to be taken sublingually as a single daily dose with the film placed under the tongue towards the base or back of the tongue on either the left or right side and allowed to dissolve completely. Cassipa is currently only available in one strength: buprenorphine 16 mg with naloxone 4 mg, and the manufacturer (Teva Pharmaceuticals) cautions that the product should only be used after the patient has been stabilized and titrated to a dose of 16 mg buprenorphine using another product.

The most commonly reported side effects associated with the use of Cassipa include numbness or a reduced sense of touch or sensation, a burning or painful sensation in the tongue, redness and swelling of the inside of the mouth, headache, nausea, vomiting, sweating, constipation, withdrawal signs and symptoms, insomnia, pain, and swelling of the lower limbs (i.e., legs). Buprenorphine is an opioid and thus carries the risk of addiction, and chronic use can lead to physical dependence. However, when used properly as part of an overall treatment program, addiction risk is minimized. Buprenorphine may be dispensed from an opioid-dependence treatment facility or prescribed for at-home use by doctors who have obtained a special waiver under the Drug Addiction Treatment Act (DATA 2000). A "Buprenorphine Treatment Physician Locator" can be found online at www.samsha.gov.

Cassipa sublingual film is not intended for use as an analgesic. Similar available products containing buprenorphine with naloxone for maintenance treatment of opioid dependence are Suboxone (sublingual film), Bunavail® (buccal film), and Zubsolv® (sublingual tablet).

Reference: https://www.accessdata.fda.gov/scripts/cder/daf/

Regulatory Update

Arizona

Rules, A.A.C. §§ R20-5-106, -1301 to -1303, -1309 to -1311, address treatment guidelines and medical treatment preauthorization. Changes to the rules include modifications to the applicability of ODG treatment guidelines to apply to all body parts and conditions, and updates to preauthorization or reconsideration requirements. The amended bills become effective for medical treatment and services provided on or after October 1, 2018.

Massachusetts

House Bill 4742 relates to electronic prescriptions, partial fills, and the Prescription Drug Monitoring Program (PDMP) under the Controlled Substances Act. The bill includes:

- The addition of a definition for "Electronic prescription"
- Requires prescribers to issue an electronic prescription for all controlled substances and medical devices
- Requires a pharmacist filling a Schedule II substance to dispense in a lesser quantity than indicated on the prescription
- Requires the establishment of regulations relating to the use of the PDMP

The provisions regarding partial fills and the PDMP became effective August 9, 2018, and provisions for electronic prescriptions become effective January 1, 2020.

Missouri

Senate Bill 826 regarding opioid prescribing limitations was adopted on August 7, 2018 with an effective date of August 28, 2018. The legislation includes the newly enacted "Opioid Reduction Act", and amends sections dealing with various licensing programs. The bill also addresses new definitions of "acute pain" and "initial prescription", as well as practitioner guidelines for issuing prescription for more than a 7-day supply of any opioid controlled substance.

Tennessee

House Bill 1831 places limitations on opioid prescriptions, and makes various changes to the requirements for prescribing, dispensing, and reporting of opioids. The bill became effective upon the governor's May 21, 2018 approval, and became effective as of July 1, 2018.

Coventry's Regulatory and Legislative Affairs (RLA) group will continue to monitor further discussion on these topics. If you have questions regarding these changes, please contact your First Script Account Manager.