

NATIONAL PBM BULLETIN

April 5, 2018

DEPARTMENT OF VETERANS AFFAIRS PHARMACY BENEFITS MANAGEMENT SERVICES (PBM), MEDICAL ADVISORY PANEL (MAP), VISN PHARMACIST EXECUTIVES (VPEs), AND THE CENTER FOR MEDICATION SAFETY (VA MedSAFE)

Alerts are based on the clinical evidence available at the time of publication. Recommendations are intended to assist practitioners in providing consistent, safe, high quality, and cost effective drug therapy. They are not intended to interfere with clinical judgment. When using dated material, the clinician should consider new clinical information, as available and applicable.

Synthetic Marijuana and Potential Risk for Bleeding

I. ISSUE

The Indiana State Department of Health issued an [Indiana Health Alert Network Advisory](#) warning that public health officials have linked synthetic marijuana use to cases of severe bleeding in Indiana and Illinois. Additionally, an [Illinois Department of Public Health Memorandum](#) recommends that pharmacies ensure sufficient vitamin K1 (phytonadione) supply for large doses to be administered for several weeks or months to manage symptoms due to the long-acting nature of this poisoning.

II. BACKGROUND

Cases reported include 16 in Illinois since March 10, and 1 in Indiana on March 27. All cases have reported using synthetic marijuana prior to illness. Specific products of synthetic marijuana (commonly known as fake pot, fake weed, legal weed, spice, K2, KD, Mind Trip, OMG, Black Giant, Matrix, Scooby Snacks, AK-47, Genie, and others) involved have not yet been identified.

III. DISCUSSION

Cases involved single agent coagulopathy with synthetic marijuana products alone, although previous published literature has suggested a possible cannabinoid-warfarin interaction. Affected patients did not have a history of warfarin use or exposure to any rodenticides containing brodifacoum, which is a lethal anticoagulant poison used for pest control. INR values ranged from 6 to greater than 20 on presentation. Prolonged hospitalization resulted due to elevated INR values despite administration of fresh frozen plasma (FFP) and intravenous vitamin K. Several cases returned to the Emergency Department after discharge because of persistent bleeding symptoms despite treatment with fresh frozen plasma (FFP) and intravenous vitamin K, suggesting a "superwarfarin" effect due to high potency and long duration of action.

IV. RECOMMENDATIONS

Per the [Indiana Health Alert Network Advisory](#):

- When treating or investigating unusual cases of bleeding (i.e., bloody nose or hematuria), providers should:
 - inquire about potential exposures to synthetic marijuana (including sites of purchase);
 - conduct INR testing;
 - identify alternative sources of vitamin K supplies, if needed.
- Until the specific products involved are identified, health care providers should consider conducting INR testing on any patients with recent synthetic marijuana use even if abnormal bleeding has not occurred.

Per the [Illinois Department of Public Health Memorandum](#), pharmacists should:

- Check stock of oral phytonadione and work with suppliers to ensure adequate supply as multiple patients may be affected and high doses ($\geq 50\text{mg/day}$) may be needed for several weeks or months to manage symptoms due to the synthetic substance's long action.
- Advise affected patients that OTC dietary supplements containing phytonadione only contain approximately 100mcg (0.1mg) and are not an effective treatment for this coagulopathy.
- Counsel affected patients that compliance with the prescribed phytonadione therapy and laboratory monitoring is necessary to prevent recurrence of bleeding complications.

V. REFERENCES

1. Indiana Health Alert Network. Synthetic Marijuana Linked to Cases of Severe Bleeding in Illinois and Indiana. Indiana State Department of Health. Available at: <https://cdn.zephyrcms.com/e97cfbad-2b69-4b7d-a7ef-e7f7908bf528/-/inline/yes/coagulopathy-ihan-3-26-18-final.pdf>. (Accessed March 28, 2018).
2. Illinois Department of Public Health. Memorandum: Ensure Sufficient Vitamin K1 (Phytonadione) Supply. Available at: <http://dph.illinois.gov/sites/default/files/publications/idph-memo-pharmacies-ensure-sufficient-vitamin-k-supply-032918.pdf>. (Accessed April 2, 2018).
3. La Rosa FG, Clarke SH, Lefkowitz JB. Brodifacoum intoxication with marijuana smoking. Arch Pathol Lab Med 1997;121:67-9.
4. Yamreudeewong W, Wong HK, Brausch LM, Pulley KR. Probable interaction between warfarin and marijuana smoking. Ann Pharmacother 2009;43:1347-53.
5. Yamaori S, Koeda K, Kushihara M, Hada Y, Yamamoto I, Watanabe K. Comparison in the in vitro inhibitory effects of major phytocannabinoids and polycyclic aromatic hydrocarbons contained in marijuana smoke on cytochrome P450 2C9 activity. Drug Metab. Pharmacokinet. 2012;27(3):294-300.

ACTIONS

- **Facility Director** (or physician designee): Forward this document to the Facility Chief of Staff (COS).
- **Facility COS and Chief Nurse Executives**: Forward this document to all appropriate providers and health care staff (e.g., primary care providers, emergency department staff, Hematology-Oncology staff, and pharmacy staff, including contract providers, etc.). In addition, forward to the Associate Chief of Staff (ACOS) for Research and Development (R&D). Forward to other VA employees as deemed appropriate.
- **ACOS for R&D**: Forward this document to Principal Investigators (PIs) who have authority to practice at the facility and to your respective Institutional Review Board (IRB).