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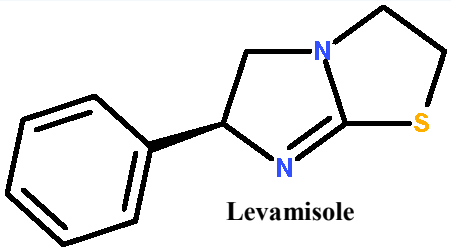
Levamisole: A Toxic Adulterant Found in Illicit Street Drugs.

GLOBAL PUBLIC HEALTH ALERT

Substance abuse treatment providers, clinicians, outreach workers, public health clinics, etc. need to be aware of the following information. A dangerous drug adulterant, levamisole, is appearing with increasing frequency in illicit cocaine powder and crack cocaine, and to some extent in heroin and fentanyl. Levamisole can cause severe adverse health effects, including a reduction in the patient's white blood cell count, a condition called agranulocytosis. **THIS IS A VERY SERIOUS ILLNESS THAT NEEDS TO BE TREATED IN A HOSPITAL. SEE ATTACHED TREATMENT AND DIAGNOSIS PLAN.**

Background: Levamisole was initially developed in the mid-1960s as a veterinary and human anti-worming drug. In 1990, it was approved by the United States Food and Drug Administration (FDA) as a therapy for the treatment of colorectal cancer, however, by 2000 it had been withdrawn from the market due to severe adverse effects described below. Since the early 2000's, levamisole has been in widespread use as an adulterating agent for illicit street drugs, especially cocaine, heroin, and fentanyl. Although its prevalence varies over time and geographically, **LEVAMISOLE HAS AT TIMES BEEN DETECTED IN UP TO 79% OF THE COCAINE STREET SUPPLY AT VARYING PERCENTAGES, UP TO 74% BY WEIGHT.**



Levamisole

Recommendations for Clinicians

- Be aware that illicit drugs may contain toxic adulterating substances that may impact the clinical presentation.
- Become familiar with the signs and symptoms associated with levamisole toxicity.
- Be aware that routine hospital drug tests will not disclose the presence of levamisole, which requires a special test.

Frequent Indicators of Levamisole Toxicity

- Unexplained fever and agranulocytosis
- Unexplained vasculitis with purple skin lesions over ear lobes, legs and thighs
- Persistent or recurrent fever and chills
- Worsening or persistent sore throat
- Worsening swollen glands
- Painful sores in the mouth or around the anus
- Frequent, persistent or worsening skin infections
- Thrush
- Other unusual infection(s)

Recommendations for MEs & Coroners

- Test for common adulterating agents in suspected stimulant- or opioid-related death cases where levamisole related findings, such as leukopenia or necrosis, are identified.

Recommendations for Forensic and Clinical Laboratories

- Develop sensitive and up-to-date testing procedures for common adulterating agents, including levamisole.
- Consider laboratory analysis of seized drug samples taken from suspected drug overdose investigations.
- Share data on drug seizures in your jurisdiction with local health departments, medical examiners, and coroners.

Levamisole Reported Internationally

Countries reporting illicit drug products adulterated with levamisole as part of the International Toxic Adulterants Database (ITAD) program and/or during The 2nd International Symposium of Forensic Drug Testing Lab Directors in Singapore.

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Health Impacts: Ingesting illicit drugs mixed with levamisole can seriously reduce a person's white blood cell count, suppressing immune function and the body's ability to fight off even minor infections.

People who snort, smoke, or inject cocaine or heroin contaminated with **levamisole can experience rapidly-developing, life-threatening infections**.

Levamisole is also associated with an array of adverse effects, many of which are immunologic/autoimmune in origin. **Classic signs of levamisole toxicity involve dangerously low levels of white blood cells, particularly granulocytes, which impacts the body's immune response and defense against infection**. Although leukopenia and agranulocytosis generally resolve upon drug discontinuation, they may on occasion prove to be fatal.

A variety of **levamisole-induced adverse cutaneous effects may occur. These range from purple-colored skin rashes (purpura), leg ulcers, and visible necrotized tissue**, and are generally vasculitic in nature. In many patients with skin necrosis, infections are common, and reconstructive surgery may be required.

The adverse symptoms of **levamisole-adulterated drugs may resolve on their own by abstaining from illicit drug use and co-administration of corticosteroids**. More severe cases can lead to further complications, leading to amputations and/or death.

People with substance abuse disorder may be more vulnerable to COVID-19 due to the drug's effects on the immune system. The problem is further exacerbated by the addition of adulterants like levamisole that results in a decrease of white blood cells that lower immunity and increase susceptibility to such infections.

Health providers should consider the possibility of exposure to cocaine adulterated with levamisole in patients with the following symptoms: nausea, vomiting, headache, metallic taste, and diarrhea. Additional effects of abdominal pain, malaise, myalgia, flu-like syndrome, rash, insomnia, sensory stimulation, dizziness, blurred vision, vertigo, impaired coordination, impaired thinking, motor aphasia, diplopia, cramps, weakness, fatigue, seizures, and epilepsy have been reported.

Clinical effects can include memory loss, lethargy, paresthesia, ataxia and even coma.

References and Related Articles:

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THE COLOMBO PLAN
FREDRIC RIEDERS FAMILY FOUNDATION
JMJ Technologies
Medical Research and Development

Levamisole Toxicity – Diagnosis and Treatment

Signs & Symptoms of Intoxication

Physical	Behavioral
Dermatitis/Skin Rash Neutropenia/Agranulocytosis Nausea/Vomiting Salivation Lacrimation Urination Diarrhea Hyperesthesia Fatigue Weakness Headache Influenza-like Symptoms Seizures (unusual)	Anxiety Irritability

Signs & Symptoms of Overdose

Physical	Behavioral
Fever Infection Salivation Lacrimation Urination Hyperesthesia Nausea Vomiting Diarrhea Weakness Headache Influenza-like Symptoms Seizures (unusual)	Anxiety Irritability

Provider Response

Physical	Behavioral
Monitor temperature & vital signs every 4 hours if indicated Pan-culture body fluids (if febrile) Provide IV fluid support and electrolyte replacement Consider broad spectrum antibiotic therapy with fever > 38°C (broad spectrum beta lactam + vancomycin) Paracetamol (acetaminophen) Loperamide 2-4 mg by mouth for diarrhea Measure WBC/differential every 1-2 days	Provide supportive care Consider small doses of benzodiazepines (diazepam 2-5 mg 2-4 times/day) for anxiety or agitation

Further treatment?

Once behavior & physical responses are stable, then determine if more treatment is needed

YES – Treatment for detoxification

Physical & Behavioral

Consider GCSF or GMCSF to stimulate WBC production if neutropenia persists

NO Treatment required

In most cases, further treatment is not required following levamisole intoxication