Drug Enforcement Administration
Diversion Control Division
Drug & Chemical Evaluation Section

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LEVAMISOLE

(Trade Name: Ergamisol®)

Introduction:

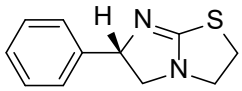
Levamisole is a veterinary drug used to treat parasitic infestation in animals. It is available as a crystalline white powder and in pastes, gels, tablets, feed premixes, and topical and injectable solutions. In Canada, it was marketed by Janssen Pharmaceuticals under the trade name Ergamisol to treat colon cancer in humans. A few cases of agranulocytosis (blood disorders), a common complication with repeated high doses of levamisole, have been reported in hospitalized patients with a history of cocaine abuse when adulterated with levamisole (CAL).

Licit Uses:

Levamisole is an anthelmintic drug approved for use in veterinary medicine in the United States. Previously, it was used in human medicine as an immunomodulator in rheumatoid arthritis and colorectal cancer therapy. It is no longer available for human use in the United States.

Chemistry:

The chemical name of Levamisole is (*S*)-6-phenyl-2,3,5,6-tetrahydroimidazo[2,1-*b*]thiazole. Two common forms of levamisole are the free base and the hydrochloride salt. The molecular formula of the free base is $C_{11}H_{12}N_2S$, which has a molecular weight of 204.3 g/mol. Its melting point is 60–61.5 degrees Celsius (°C), and it is not soluble in water. The hydrochloride salt is soluble in water and melts at 227–229 °C. The Chemical Abstract Service (CAS) number of the free base is 14769-73-4 and the hydrochloride salt is 16595-80-5. The chemical structure of levamisole is shown below:



Pharmacology:

Levamisole acts as an antiparasitic, immunomodulator, and adjuvant in colorectal cancer. Levamisole restores depressed immune function by stimulating antibody formation and enhances T-cell response by stimulating T-cell activation and proliferation. Antiparasitic action may be tied to its agonistic activity at nicotinic receptors in the muscle of nematodes, resulting in spastic paralysis. The net effect is a paralyzing of the worm, which is then expelled alive.

Levamisole is rapidly absorbed from the gastrointestinal tract, extensively metabolized in the liver, and excreted mainly by the kidneys (70% over 3 days). Its plasma elimination half-life is 3–4 hours. Due to the short elimination half-life, blood levels of levamisole fall more rapidly and go unnoticed in toxicological examination. Levamisole is metabolized into an active metabolite that has amphetamine-like effects, known as aminorex. Aminorex is a schedule I substance and can enhance the stimulant-like effects of cocaine.

Data from few clinical studies indicate that the consumption of 50–200 mg/day of levamisole causes agranulocytosis in 0.08–5% of the studied population. Agranulocytosis is an acute blood condition that leaves patients unable to fight off infections resulting from decreased neutrophil count (neutropenia). This condition has been reported world-wide in CAL abusers. Higher than recommended doses of levamisole are reportedly associated with an increased incidence of autoantibody mediated agranulocytosis. Symptoms of agranulocytosis include sore throat, persistent or recurrent fever, swollen glands, and skin infections. Levamisole may interfere with the breakdown of alcohol and cause unwanted side effects, such as flushing, irregular heartbeat, low blood pressure, sweating, nausea, and vomiting.

User Population:

Levamisole is mainly encountered in combination with cocaine as an adulterate. Therefore, the levamisole user population includes cocaine abusers.

Toxicity:

Symptoms of levamisole toxicity mimic organophosphate toxicity (salivation, lacrimation, urination and defecation, hyperesthesia, seizures, and irritability). There is no antidote for levamisole toxicity.

Regulatory Guidance:

The World Health Organization reviewed hematological studies in animals and humans and derived acceptable daily intake for levamisole as 0.006 mg/kg body weight. This suggests that a person can ingest 0.36 mg of levamisole per day over a lifetime without any appreciable risk.

Illicit Distribution:

The Drug Enforcement Administration's National Forensic Laboratory Information System (NFLIS) Drug database collects scientifically verified data on drug items and cases submitted to and analyzed by participating federal, state, and local forensic drug laboratories. NFLIS-Drug received 1,211 reports of levamisole in 2021; 1,401 in 2022; 433 in 2023; and 89 in 2024 (reports still pending). In total, NFLIS-Drug received over 24,000 reports of levamisole since its first report in 2003.

Control Status:

Levamisole is not controlled under the Controlled Substances Act.

Comments and additional information are welcomed by the Drug and Chemical Evaluation Section; Fax 571-362-4250, Telephone 571-362-3249, or Email DPE@dea.gov.