Etizolam: Information for Health Care Providers

June 2019

What is etizolam?

Etizolam is a short-acting thienodiazepine derivative that was developed in the 1980s as an alternative to benzodiazepines (BZDs). Etizolam has properties similar to diazepam. It is structurally different but pharmacologically similar to BZDs. It is typically used for in vitro research and, in some cases, has been used for short-term treatment of insomnia, anxiety disorders, depression, and as a muscle relaxant.

Benzodiazepines (BZDs)

BZDs are used therapeutically as anxiolytics, muscle relaxants, sedative-hypnotics, amnesics, and anticonvulsants. These effects are produced by enhanced activity of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA) in the brain.

BZDs bind to BZ receptors to facilitate binding of GABA to its respective receptors. Numerous BZ receptor types have been identified, which produce different effects when active, and BZDs act non-selectively at these sites, resulting in therapeutic and adverse effects. BZDs are frequently combined with alcohol or opioids when used casually.

Pharmacokinetics & Detection

Etizolam is well-absorbed once in the body with 93% protein binding. Time to peak effects is 3.3 hours and half-life elimination is 6.3 hours. It is metabolized the liver via CYP3A4 and CYP2C9, and excreted in the urine (53% primarily as metabolites). Detection of the ingested parent drug is not always possible due to extensive hepatic metabolism, and testing may rely on identification of metabolites in the blood with long half-lives.

Management of Poisoning/Overdose

Presentation of etizolam poisoning can overlap with presentation of opioid poisoning and include signs and symptoms of central nervous system (CNS) and respiratory depression: sedation, dizziness, amnesia, ataxia, slurred speech, lethargy, respiratory difficulties. When severe poisoning can result in coma, hypotension, hypothermia and respiratory failure. When consumed through different routes, such as oral ingestion, intranasal or intravenous, clinical presentations remain the same, though onset, duration and severity may vary due to differences in pharmacokinetics.

Treatment of poisoning or overdose on etizolam should primarily be focused on the clinical presentation of the patient and not the substance ingested or consumed. Stabilization is priority: evaluating and correcting immediate life-threatening complications of the patient (e.g., airway, breathing, circulation). Supportive care with emphasis on respiratory support, supplemental oxygen administration, and aspiration prevention is primary treatment.

Harm Reduction Services Team
harm.reduction@ahs.ca | ahs.ca/harmreduction

Alberta Health Services

In some cases, if within 1 hour of ingestion, and the patient is not intubated with a Glasgow Coma Scale score of 15, decontamination via single-dose activated charcoal may be an option. Treatment via use of the BZD antidote flumazenil is not recommended. Flumazenil can reverse the CNS depression associated with therapeutic use of BZDs for anesthesia and sedation, however safety of use in poisoning, especially if the patient is comatose and engaging in polysubstance use, is controversial due to risk of seizure. For patients who are chronically maintained, physiologically dependent, have a history of underlying seizure disorder or have co-ingested a proconvulsant (e.g., tricyclic antidepressant) the risk of seizure induced by flumazenil is a concern.

Patients with severe and persistent CNS depression, hemodynamic instability and/or respiratory depression require hospital admission and intensive care support.

Etizolam in Alberta

Etizolam has been detected in a number of cases in Alberta. It was first reported by the Office of the Chief Medical Examiner (Toxicology Department) in 2016. In every case where etizolam has been identified, at least one other substance was also present. Regarding illicit substances, cocaine was most frequently detected in etizolam positive cases. In 2019, reports from British Columbia showed etizolam being present in opioids and complicating opioid overdose response in the community setting.

Patients with suspected co-ingestion with opioids can be given naloxone with supportive care. As always, treatment is recommended for the patient's symptoms and clinical presentation and not the poison or substance ingested.

References

Banerjee, D. (2018). Etizolam withdrawal catatonia: the first case report. *Asian Journal of Psychiatry, 37*, 32-33.

Wolters Kluwer Clinical Drug Information, Inc. (2018). Benzodiazepines, Blood, Screen and Confirmation. Retrieved from Lexicomp Database. http://online.lexi.com.ahs.idm.oclc.org/lco/action/doc/retrieve/docid/51/6523322

Wolters Kluwer Clinical Drug Information, Inc. (2019). Benzodiazepines (Lexi-Tox). Retrieved from Lexicomp Database. http://online.lexi.com.ahs.idm.oclc.org/lco/action/doc/retrieve/docid/lexier/1253640#rel-labdiag

Wolters Kluwer Clinical Drug Information, Inc. (2019). Etizolam (Martindale: The Complete Drug Reference). Retrieved from Lexicomp Database. http://online.lexi.com.ahs.idm.oclc.org/lco/action/doc/retrieve/docid/martindale_f/1352579

Wolters Kluwer Clinical Drug Information, Inc. (2018). Etizolam (AHS Patient Education – Adult Medication). Retrieved from Lexicomp Database. http://online.lexi.com.ahs.idm.oclc.org/lco/action/doc/retrieve/docid/pated_f/5552513