

Flumazenil (Romazicon®): A Risky Antidote

Benzodiazepines are widely used as sedative-hypnotic agents and are sometimes used for their anticonvulsant and muscle-relaxant properties. Overdoses are a common occurrence with 65,998 cases reported to U.S. poison centers in 2004. In contrast to other sedative-hypnotics, benzodiazepines have a high degree of safety, even in massive overdoses. The clinical course is characterized primarily by CNS depression. When combined with other sedatives, most frequently alcohol, coma and respiratory depression may be seen. Deaths are rare.

Most patients with benzodiazepine overdose can be managed in the ED with activated charcoal and supportive care and discharged home or referred for psychiatric evaluation once the patient becomes arousable. **Flumazenil (Romazicon®)** is a specific benzodiazepine antagonist that rapidly reverses benzodiazepine-induced CNS depression, but does not consistently reverse respiratory depression. Although it has been safely used in unintentional overdoses in children and to reverse conscious sedation in hospitalized patients, **flumazenil has no role in the management of an unknown or intentional ingestion. Flumazenil has the potential of inducing withdrawal and seizures in patients who are benzodiazepine-dependent.** Other possible risk factors for flumazenil-induced seizures include:

- concurrent major sedative-hypnotic drug withdrawal
- history of seizures, myoclonic jerking or seizure activity prior to flumazenil administration
- concurrent cyclic antidepressant, thioridazine or mesoridazine poisoning (may result in dysrhythmias or seizures)
- ingestion of other drugs that are capable of inducing seizures (cocaine, theophylline, carbamazepine, chloral hydrate, chloroquine...).

Benzodiazepines

alprazolam (*Xanax*)
chlordiazepoxide (*Librium*)
clonazepam (*Klonopin*)
chlorazepate (*Tranxene*)
diazepam (*Valium*)
estazolam (*ProSom*)
flurazepam (*Dalmane*)
lorazepam (*Ativan*)
midazolam (*Versed*)
oxazepam (*Serax*)
prazepam (*Centrax*)
quazepam (*Doral*)
temazepam (*Restoril*)
triazolam (*Halcion*)

*flunitrazepam (*Rohypnol*)
is not approved for use in
the U.S.

The risks of using flumazenil in most overdose patients outweigh the potential benefits. Call the Maryland Poison Center for assistance in evaluating benzodiazepine overdoses and before giving flumazenil.

DID YOU KNOW THAT... Flumazenil-induced seizures are not likely to respond to benzodiazepines?

Flumazenil occupies benzodiazepine receptor sites; therefore, seizures that occur as a result of flumazenil administration are not likely to respond to benzodiazepines typically used for drug-induced seizures, such as diazepam and lorazepam. Phenytoin is often ineffective when used for drug and toxin-induced seizures. Phenobarbital 10-20 mg/kg IV is the preferred anticonvulsant.



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If you do not wish to receive faxes or emails from the Maryland Poison Center, call 410.706.7604 or circle your fax number and fax this back to 410.706.7184. Supported by Maryland Department of Health and Mental Hygiene

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