

Flumazenil

Benzodiazepines have numerous therapeutic indications and are also used recreationally. While most benzodiazepine overdoses are not serious, toxic effects include drowsiness, slurred speech, nystagmus, hypotension, ataxia, and, less frequently, coma, respiratory depression and cardio-respiratory arrest.

Mechanism/Indications: Flumazenil is a competitive antagonist at the benzodiazepine site on the GABA_A receptor. Flumazenil is effective at reversing the CNS depression associated with benzodiazepine overdose in select populations. Benzodiazepine naive patients with an acute overdose of only a benzodiazepine are appropriate candidates for flumazenil. Flumazenil may be effective in acute benzodiazepine overdoses in children. Flumazenil can be beneficial to reverse over-sedation after benzodiazepines are administered for procedural sedation.

Adverse Effects/Contraindications: Adverse effects include dizziness, nausea, vomiting, diaphoresis, headache, blurred vision, anxiety and pain at injection site. Flumazenil's use is limited as the risks may outweigh the benefits in a patient who has taken an intentional overdose. Flumazenil has numerous relative contraindications including benzodiazepine dependence, co-ingestion of seizure or arrhythmia causing agents such as cyclic antidepressants, or seizure history. A benzodiazepine-dependent patient who is administered flumazenil can experience acute withdrawal (hyperexcitability, tachycardia, and/or seizures). Likewise, it may be harmful in patients who have taken stimulants or pro-convulsants. If flumazenil is given in mixed ingestions, the neuro-protective effects of the benzodiazepine will be removed by flumazenil and can allow pro-convulsive properties to predominate. Treating these seizures becomes complicated as benzodiazepines are first-line anti-convulsants yet cannot be used due to receptor blockade. Patients Resedation following flumazenil administration can occur due to its short duration of action.

Dosing: Flumazenil is available as a clear colorless intravenous solution supplied as 0.1 mg/mL in 5 and 10 mL vials. Initial dose is 0.2 mg IV over 30 seconds. Give an additional 0.3 mg IV over 30 seconds if the desired response does not occur within 30 seconds. Repeat doses of 0.5 mg IV may be given at 1 minute intervals as needed up to 3 mg total dose. The pediatric dose for children 1 year or older is 0.01 mg/kg IV (up to 0.2 mg) over 15 seconds. May repeat 0.01 mg/kg IV (up to 0.2 mg/dose) at 1 minute intervals as needed; maximum total dose is 0.05 mg/kg or 1 mg, whichever is lower. Its short duration of action (20-120 minutes) lends itself to multiple dosing or continuous infusion to treat recurrent symptoms.

For more on flumazenil:

- Seger DL. Flumazenil - Treatment or Toxin. *Clin Toxicol* 2004; 42:209-216.
- Kreshak AA, et al. A poison center's ten year experience with flumazenil administration to acutely poisoned patients. *J Emerg Med* 2012;43(4):677-82.
- Veiraiah A, et al. Flumazenil use in benzodiazepine overdose in the UK: a retrospective survey of NPIS data. *Emerg Med J* 2012;29(7):56-59.
- Howland MA. Antidotes in Depth: Flumazenil. In: Hoffman RS, Howland MA, Lewin NA Nelson LS, Goldfrank LR, editors: *Goldfrank's Toxicologic Emergencies*. 10th ed. New York NY, 2015;1013-1017.