Diazepam

**Generic Name:** Diazepam  
**Trade Name:** Valium, Antenex, Diazemuls, T-Quil, Vazepam, Zetran  
**Drug Class:** Benzodiazepine derivative. BZD 3, Long Acting, Lipid Soluble  
**Controlled Substance:** Schedule IV  
**Pregnancy Class:** D

**Action**

Diazepam acts on “GABA Gates” or receptors. The GABA receptor is an inhibitory channel within the ascending central nervous system. Diazepam is a GABA agonist, which binds specifically to the benzodiazepine receptors of GABA which then inhibits/alters the neurological activity.

When Diazepam binds, it hyperpolarizes the post synaptic neuron due to GABA’s regulatory control over the Chloride channels. Chloride is a negatively charged ion that plays a major role in neurological impulse transmission. This enhanced GABA activity allows for an influx of Chloride into the post synaptic neuron. This negatively charged cation, which alters the neurological activity, slows down nerve impulses by decreasing the action potential and decreasing the firing rate.

Diazepam acts on areas of the Limbic, Thalamus and Hypothalamus because of its GABA enhancing action. Administering Diazepam to a patient in seizure or showing excessive signs of neurologic activity (cocaine, excited delirium, CNS stimulants) is a beneficial part of the treatment plan. When it binds to the benzodiazepine receptor it causes hyperpolarization. The hyperpolarization (via increased amount of intracellular chloride) decreases the membranes resting action potential making the neuron relatively negatively charged.

This will increases the amount of stimulus needed to bring the membrane to its depolarization threshold, or “Raising seizure threshold”. This much, the
same way antiarrythmics (i.e.: Lidocaine) work by altering the action potential in cardiac pacemaker cells.

Diazepam’s sedative properties results from its action on the GABA receptors and produce an inhibitory effect on the ascending CNS. Diazepam also results in the depression of the Reticular Activating System which controls level of consciousness.

**Onset**
- Oral -> 30min, Peak plasma levels after up to 2hrs
- IV -> 1-5min, Peaks Immediately with IV administration.
- IM -> 15-30 min onset of action

Diazepam has a duration of action of approximately 3hrs, and a half life of 20-70hrs.

**Routes of Administration**

**Intravenous**
- Give drug slowly, as to not cause reactions at the administration site.
- Diazepam interacts with plastic containers and IV tubing, significantly decreasing availability of drug delivered. Do not mix or dilute with other solutions or drugs in a syringe or infusion container.
- Emergency equipment should be readily available (i.e. Airway protection, and Oxygenation equipment)

**Intramuscular**
- IM injections are painful and erratically absorbed. If IM route is used, inject deeply into deltoid muscle for maximum absorption

**Per-Rectum**
- Dose should be doubled

**Indications**
- Anxiety
- Tension
- Alcohol withdrawal
- Anticonvulsant
- Procedural Sedation in:
  - Cardioversion
  - Gastroscopy
  - Esophagoscopy
- Adjunct in
  - CP
  - Paraplegia
  - Tetanus
Contraindications

- Hypersensitivity/Allergy to benzodiazepines
- Shock
- Narrow angle Glaucoma
- ETOH intoxication, Alcohol also binds to the GABA Receptors of the CNS; administering Valium when a person is severely intoxicated will cause a synergistic effect, and increase CNS depression.

Adverse Reactions

**CNS**
- Drowsy
- Slurred speech
- Tremor
- Transient amnesia
- Fatigue
- Ataxia
- Headache
- Insomnia

**Cardiovascular**
- Hypotension
- CV Collapse
- Bradycardia

**EENT**
- Diplopia
- Blurred Vision
- Nystagmus

**GI/GU**
- Nausea
- Constipation
- Incontinence or urine retention
- Altered libido

**Respiratory**
- Respiratory depression

**Other**
- Skin rash, phlebitis, jaundice, neutropenia.
Interactions

- Cimetidine – Increased sedation
- Digoxin – Increased Serum Levels
- Alcohol/CNS depressants – increased CNS depression
- Phenobarbital – increased effects of both drugs
- Smoking – Causes increased clearance of benzodiazepines
- Diazepam potentiates the antihypertensive effects of thiazide and other diuretics.
- Diazepam potentiates the effects of the muscle relaxant effects of d-tubocuraine and gallamine
- Ranitidine causes decreased renal absorption of Diazepam
- Isoniazid and Fluoxetine both increases the half life of Diazepam

Overdose

Although not usually fatal when taken alone, a diazepam overdose is considered a medical emergency and generally requires the immediate attention of medical personnel. The antidote for an overdose of diazepam (or any other benzodiazepine) is flumazenil (Anexate®). This drug is only used in cases with severe respiratory depression or cardiovascular complications. Because flumazenil is a short-acting drug and the effects of diazepam can last for days, several doses of flumazenil may be necessary. Artificial respiration and stabilization of cardiovascular functions may also be necessary. Although not routinely indicated, activated charcoal can be used for decontamination of the stomach following a diazepam overdose. Induced vomiting is contraindicated. Dialysis is minimally effective.

Elimination

Diazepam is metabolized by the liver and is specifically metabolized into the active metabolites desmethyldiazepam, oxazepam, and temazepam. Diazepam and metabolites are then excreted in the urine.