

Pyridoxine

Pyridoxine (vitamin B6), a water-soluble vitamin, is an antidote used for isonicotinic acid hydrazide (isoniazid), *Gyromitra esculenta* mushrooms, hydrazine, and methylated hydrazines. All of these substances precipitate seizures by competitive inhibition of pyridoxal-5'-phosphate (PLP), which is involved in the production of γ -aminobutyric acid (GABA). Seizure activity increases anaerobic metabolism, resulting in lactic (metabolic) acidosis. In addition, pyridoxine is used as adjunctive therapy in ethylene glycol poisoning.

Mechanism/Indications: Pyridoxine is metabolized by pyridoxal kinase to its active metabolite, PLP. PLP acts as a cofactor in converting glutamate to GABA. Thus, pyridoxine increases GABA synthesis. It is indicated for the prevention and treatment of seizures, metabolic acidosis and/or coma in poisonings caused by isoniazid, hydrazines and *Gyromitra esculenta* mushrooms. Pyridoxine is a cofactor in ethylene glycol metabolism. It promotes the formation of nontoxic metabolites.

Adverse effects/Contraindications: Typical doses for these indications are well-tolerated. Pyridoxine may cause a sensory axonal neuropathy, decreased folic acid concentrations, headaches, and drowsiness when taken chronically or in massive single doses. Large intravenous doses (>1 g/kg) have precipitated seizures in animals.

Dosing: The dose of pyridoxine should equal the dose of isoniazid taken, gram-for-gram given intravenously, up to 5 g total. If the dose of isoniazid is unknown, 5 g of pyridoxine is an appropriate dose. The maximum dose is 5 g or 70 mg/kg in a child. It is administered at 0.5 g/min by intravenous (IV) route until seizures subside or a maximum dose is reached. If seizures persist, this dosing schedule may be repeated until seizures stop. If seizure activity ceases prior to finishing the initial dose, the remaining amount of pyridoxine should be infused over 4-6 hours. The same dosage applies to poisonings by *Gyromitra esculenta* mushrooms and hydrazines. Because pyridoxine is only available as 100 mg/mL in 1 mL vials, 50 vials are required to administer a 5 g dose. For ethylene glycol poisonings, the pyridoxine dose is 100 mg/day IV.

Note: If IV pyridoxine is unavailable, the oral dosage form may be given, although this is not the preferred method.

For more on pyridoxine:

- Burda AM, Sigg T, Haque D, Bardsley CH. Inadequate Pyridoxine Stock and Its Effect on Patient Outcome. *American Journal of Therapeutics* 2007;14(3):262-264
- Howland MA. Antidotes in Depth: Pyridoxine. In: Hoffman RS, Howland MA, Lewin NA, et al, eds: *Goldfrank's Toxicologic Emergencies*. New York NY, 2015;797-799.

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