

Hydroxocobalamin (Cyanokit®)

Cyanide binds to the iron in mitochondrial cytochrome oxidase a-a₃, a vital enzyme in the last step of oxidative phosphorylation, thus preventing the transfer of electrons to oxygen and the cell's ability to aerobically produce energy. This impairment of oxygen utilization then causes metabolic acidosis, cyanosis, seizures, hypotension, bradycardia, dysrhythmias, pulmonary edema, apnea, stupor, and coma, and can rapidly lead to death if not treated. Depending on its form, cyanide is toxic via ingestion, inhalation and dermal exposure.

Mechanism/Indications: Hydroxocobalamin has a higher binding affinity for cyanide than cytochrome oxidase and exerts its antidotal effect by binding to cyanide to form cyanocobalamin (vitamin B12). The body then excretes cyanocobalamin renally.

Adverse Effects/Contraindications: There are no contraindications and since cyanide poisoning is life-threatening, the benefit of hydroxocobalamin use often outweighs any risk. The most notable adverse effects of hydroxocobalamin are red urine and dermal erythema, both of which can last for days. Transient hypertension can occur; blood pressure generally returns to baseline within four hours after the infusion without the use of antihypertensives. Other possible adverse effects include decreased lymphocyte count, nausea, headache, hypersensitivity reactions, rash, photosensitivity and injection site reactions. Due to the deep red color of hydroxocobalamin, it can interfere with colorimetric methods used in laboratory measurements such as aspartate aminotransferase, total bilirubin, creatinine, magnesium, and serum iron. It also may interfere with co-oximeter testing of carboxyhemoglobin, methemoglobin and oxyhemoglobin.

Dosing: Hydroxocobalamin is parentally administered. It is available in Cyanokit which includes one 250 mL vial containing 5 g of lyophilized hydroxocobalamin, an IV infusion set and instructions. Hydroxocobalamin is reconstituted with 250 mL of normal saline; if normal saline is unavailable lactated ringers or D5W may be used. The dose should be used within 6 hours of reconstituting. Before administering, each vial should be inverted repeatedly for at least 60 seconds without shaking. The final solution should be dark red and without particulate matter. The 5 g dose is given intravenously over 15 minutes. If needed, a repeat of 5g IV over 15 min to 2 hours can be used. Uncontrolled studies show that doses more than 10g have not improved survival rates. The pediatric dose is 70mg/kg up to the adult dose.

For more on hydroxocobalamin:

- DesLauriers C, Burda A, Wahl M. Hydroxocobalamin as a Cyanide Antidote. *Am J Therapeutics* 2006; 13:161-165.
- Shepherd G, Velez L. Role of Hydroxocobalamin in Acute Cyanide Poisoning. *Ann Pharmacotherapy*. 2008; 42:661-669.
- Howland MA. Antidotes in Depth: Hydroxocobalamin In: Hoffman RS, Howland MA, Lewin NA Nelson LS, Goldfrank LR, editors: *Goldfrank's Toxicologic Emergencies*. 11th ed. New York NY, 2018; 1618-21.