

Management of Cyanide Exposure

Review of hydroxocobalamin

by Donna Lotzer, RPh, CSPI

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Cyanide has been used as an agent for suicide, homicide, terrorism and chemical warfare and can contribute to the death of victims of smoke inhalation in enclosed space fires.^{2,4} In fact, in the United States, smoke inhalation causes as many as 10,000 fatalities each year. While carbon monoxide has historically been viewed as the leading cause of death in smoke inhalation fatalities, recent research in the United States and Europe suggests that cyanide, too, is an important part of smoke inhalation morbidity and mortality.⁵ Cyanide poisoning can also occur from overdoses of nitroprusside, industrial accidents, swallowing artificial nail removers with acetone-trile, as well as toxic plant ingestions (cassava, stone fruit pits, laetrile).^{5,6} The list of occupations where cyanide compounds are used is extensive, numbering 72 in one citation.⁷

The time from initial exposure to cyanide and symptom onset can vary from seconds to hours, depending primarily on the route and concentration of the cyanide.⁷ Moderate to high concentrations can cause loss of consciousness in seconds, and respiratory depression and cardiac arrest follow in minutes. However ingestion of acetonitrile may mean that no symptoms are evident for 6-14 hours, because it requires metabolism to inorganic cyanide before it produces toxic effects.⁶

Critical steps in pre-hospital management of a victim with cyanide exposure include removal from the contaminated environment as appropriate, aggressive supportive measures including advanced cardiac life support (CPR, 100% oxygen, ECG monitoring), administration of IV fluids and vasopressors for hypotension, sodium bicarbonate for metabolic acidosis, and anticonvulsants, epinephrine and antiarrhythmics as needed.^{4,7,8} For oral exposures, activated charcoal may be indicated. For dermal contact, washing with copious amounts of water is appropriate after clothing and jewelry removal. After these steps have been taken, use of an antidote should be considered. Ideally this is the point at which an initial dose of hydroxocobalamin (Cyanokit, Dey Pharmaceuticals, Inc.) would be administered to patients. The older cyanide antidote kit (CAK) was not considered suitable for pre-hospital use in most cases and few EMS units even carried that product.^{8,9} In contrast, Cyanokit is relatively easy to administer, and the side effect profile is favorable for use in this setting.

The effectiveness of hydroxocobalamin as a cyanide antidote was first demonstrated in 1952.² In Europe, where hydroxocobalamin has been available for almost 50 years and has been ap-

Summary

Indications. Hydroxocobalamin (Cyanokit, Dey Pharmaceuticals, Inc) is approved by the Food and Drug Administration (FDA) as an antidote for use in known or suspected cyanide poisoning in adults.¹

Monitoring Parameters. Treatment should be initiated if symptomatic patients present with a history of smoke inhalation or possible cyanide exposure.²⁻³ This drug would be used in conjunction with advanced cardiac life support (ACLS) guidelines. Parameters that should be monitored to evaluate the efficacy of therapy include the following: improvement in airway, oxygenation and hydration, along with cardiac and neurologic status. In addition the clinician should monitor for resolution of the patient's symptoms and for adverse effects of hydroxocobalamin. This may involve observing for chromaturia, erythema, skin rash, increased blood pressure, headache, nausea and infusion site reactions.

Dose. A starting dose of 5 g is administered as an intravenous infusion over 15 minutes. Depending on the severity of the poisoning and the response to the first dose, an additional dose may need to be given. This would be another 5 g given over 15 minutes to two hours as clinically indicated. Each 2.5 g vial must be reconstituted with 100 mL of diluent. The recommended diluent is normal saline although dextrose 5% or Lactated Ringers can also be used.¹

Pediatrics. Safety and efficacy in pediatric patients has not been established, although in non-US marketing experience, a dose of 70 mg/kg has been used to treat pediatric patients.

Geriatrics. Safety and efficacy in patients aged 65 and older is similar to that in younger patients. No dose adjustment is needed in geriatric patients.

Pregnancy Category. C. Animal studies are insufficient with respect to effects on pregnancy. There are no adequate and well-controlled studies in pregnant women. Hydroxocobalamin should be used in pregnancy if potential benefits outweigh possible risk to the fetus. There are limited cases of use in pregnant women without reports of adverse effects to the fetus.

Breast Feeding. It is not known if hydroxocobalamin is excreted in human milk. There are no data to determine when breastfeeding may be resumed following administration of hydroxocobalamin. Since this drug is being administered in a life-threatening situation, breast-feeding is not a contraindication to its use.

Renal Insufficiency. The safety and efficacy of hydroxocobalamin have not been studied in patients with renal impairment. The drug and its complexed form of cyanocobalamin are eliminated unchanged in the urine.

Hepatic Insufficiency. The safety and efficacy of hydroxocobalamin have not been studied in patients with hepatic impairment.

Stability. This drug comes in a lyophilized form and while it is recommended to be stored at USP Controlled Room Temperature, it remains stable when exposed to elevated or freezing temperatures.¹ When tested at temperatures ranging from 41° F to 104° F it was stable for 15 days. When tested at temperatures ranging from 41° F to 140° F it was stable for at least 4 days. When tested at temperatures ranging from -4° F to 104° F in freeze/thaw cycles, it was stable for 15 days. Once reconstituted it can be kept at temperatures not exceeding 104° F for no more than 6 hours, after which it should be discarded. The kit has an expiration date of 30 months from production.

proved in France for use in cyanide poisonings since 1996, it has been used mostly in smoke inhalation victims in fire situations, where it has demonstrated clear benefits, especially when given in a pre-hospital setting.^{3,10,11}

PHARMACOLOGY

Cyanide is an extremely toxic poison.¹ Poisoning is caused by the inability of cells to use oxygen rather than by deficient oxygen delivery or supply.¹² By contrast, carbon monoxide binds to hemoglobin to prevent the binding of oxygen, disrupting delivery to the tissues. Exposure to a high dose of cyanide by inhalation, ingestion, or skin and mucous membrane absorption can be fatal within minutes due to the inhibition of cytochrome oxidase resulting in termination of cellular respiration, respiratory muscle failure, and cardiac arrest. Signs and symptoms of acute systemic poisoning may be evident within minutes to hours depending on the route and extent of cyanide exposure. The estimated 30-minute adult median lethal concentration of hydrogen cyanide gas (HCN) is 200 ppm, while the five-minute median lethal concentration is 680 ppm. In the presence of water or water vapor HCN is released. This may translate to an estimated lethal oral dose of HCN (in solution) of 50 mg.¹³ For potassium or sodium cyanide salts, the lethal oral dose is estimated at 200-300 mg. Hydroxocobalamin binds with cyanide on an equimolar basis (one hydroxocobalamin molecule binds one cyanide molecule) to form cyanocobalamin (vitamin B₁₂) and thereby detoxify the cyanide. This compound is then excreted in the urine. It appears that 5 g of the antidote will effectively treat patients poisoned with up to 250 mg cyanide without the need for an additional dose.^{4,14}

PHARMACOKINETICS

Following IV administration of hydroxocobalamin, significant binding to plasma proteins and other compounds occurs, forming various cobalamin-(III) complexes by replacing the hydroxo ligand.¹ The predominant mean half-life of free and total cobalamins-(III) was found to be approximately 26-31 hours at both the 5 g and 10 g dose. The mean total amount of cobalamins-(III) excreted in the urine over 72 hours was about 60% of a 5 g

dose and about 50% of a 10 g dose of hydroxocobalamin. The majority of urinary excretion occurred during the first 24 hours, but chromaturia (red-colored urine) was observed within the first two hours after administration and for up to 35 days following IV infusion.¹⁵ Skin redness was also observed within a mean time of 13 minutes from the start of the infusion for both 5 g and 10 g doses. This redness resolved, on average, in 4.1-8.6 days after the end of the infusion.

CLINICAL TRIALS

The FDA approved Cyanokit under the Animal Efficacy Rule, which allows for drug approval based on evidence of effectiveness in animals when adequate trials cannot be conducted ethically or feasibly in humans (although safety was established in humans).¹⁵⁻¹⁷ In humans the published efficacy data consists of one prospective and one retrospective study in victims of smoke inhalation, as well as case reports.^{3,10}

Smoke inhalation

A prospective open-label noncomparative trial of smoke inhalation victims was undertaken in Paris, France from 1987 – 1994.¹¹ The Paris Fire Brigade responded to the calls with a mobile ICU, staffed with a physician and nurse. They treated 69 patients, with a mean age of 49 years. Cyanide poisoning was assumed in patients with evidence of soot in the mouth, nose or expectorations, and who had neurologic impairment. Mean time to initiation of care was ten minutes from the time of the fire call. In addition to standard resuscitation measures, hydroxocobalamin was administered IV in doses ranging from 5-15 g, at the fire scene and/or in ICU at the one hospital where all were admitted. Blood for cyanide levels and carbon monoxide determination was collected prior to antidote administration. Patients were excluded if they were obviously pregnant women, those with burns over more than 20% of body surface area, and those who had suffered multiple trauma. Supportive therapies were provided according to need and physician protocols and included hyperbaric oxygen in 57 patients.

Of the 69 patients, 37 were initially comatose and 14 were in cardiopulmonary arrest. In those proven to have toxic cyanide

TABLE 1. SIGNS AND SYMPTOMS OF CYANIDE POISONING

Adapted from 6,8,9,19

Early manifestations	Later manifestations	Possible Findings	Laboratory Abnormalities
Dizziness	Seizures	Normal to pink or red skin color	Elevated plasma lactate (if ≥8-10 mmol/L)
Headache	Coma	Bright red retinal veins and arteries	Metabolic acidosis
Weakness	Respiratory depression	Breath smells like bitter almonds	High venous oxygen (if AV saturation difference <10 mm Hg)
Anxiety	Paralysis	Soot in mouth and nose (fire victims)	
Flushing	Apnea		
Perspiration	Respiratory arrest		
Dyspnea	Hypotension		
Tachypnea	Cardiac arrhythmias		
Tachycardia	Noncardiogenic pulmonary edema		
	Cardiovascular collapse		

levels, 67% survived. In total, 72% of all victims admitted to ICU survived. Neurological recovery (resolution of neurological signs including agitation, mental confusion, and altered mental status as judged by Glasgow Coma Scale scores) was observed in 82% of surviving patients. Hydroxocobalamin was well tolerated in all patients, whether or not they were proven to be cyanide poisoned. Administration was associated with an increase in blood pressure and improvement of hemodynamic status, even for those found in cardiac arrest. Adverse effects as noted by the physicians included chromaturia, red skin discoloration, and hypertension. There was no long-term, post-discharge follow-up of patients to assess delayed neuropsychiatric sequelae. Among the 19 patients who died, 13 had suffered cardiac arrest at the scene. Five others died of septic shock and one from pneumonia. Limitations to this study included the absence of a control group (for obvious reasons), the open-label design, and the possible impact of multiple other interventions, including hyperbaric oxygen. Length of time of smoke exposure was not known in these victims. Victims had also been exposed to carbon monoxide and other unknown toxins in the fire setting.

A retrospective study of victims of smoke inhalation from closed-space fires in Paris, France has been published.¹⁰ A total of 101 patient charts were reviewed, covering the period from 1995-2003. Patients were initially managed by the Paris Fire Brigade, who administered supportive and antidotal therapies prior to and during transport to hospital. It was assumed that patients had concurrent cyanide and carbon monoxide poisoning and blood cyanide levels were not measured. There were no patient exclusions in this study. The drug was administered as soon as medically feasible at the scene of the fire. The mean time from initial care to antidotal treatment was 14 minutes. Patients received doses of hydroxocobalamin ranging from 1-10 g with a mean dose of 4.7 g.

The main retrospective efficacy measure was survival rate. Subgroups of victims included those with cardiac arrest (38), those in shock (5), and those with neurological impairment (46). Among the 72 victims for whom outcomes were known, 30 (41.7%) survived after being given hydroxocobalamin. Of the 38 victims found in cardiac arrest, 21 had a return of spontaneous circulation in the field. Most of these (19 of 21) however later died in ICU. In total only two of those found in cardiac arrest survived. In 12 hemodynamically unstable patients, nine improved after hydroxocobalamin was given. Glasgow Coma Scale ratings improved in 52 nonsedated victims. Forty-nine patients had been given sedating drugs so their score could not be calculated. Adverse effects included chromaturia and red skin discoloration, with one person developing a skin rash. This individual was an AIDS patient and the relationship is not certain. It is suggested that hydroxocobalamin is most effective when given prior to cardiac arrest.

Case studies - cyanogenic compounds, suicidal and occupational exposures

A retrospective review was done of hospital records at two locations in France for cases of cyanide poisoning, excluding smoke inhalation exposures, which were managed with hydroxocobalamin as first-line antidotal therapy.³ Fourteen qualifying patients were located from 1988 to 2003. Twelve of the 14 cases were

suicide attempts. Patients ingested cyanide salts in 10 cases, while one person each took acetonitrile and mercuric cyanide. One exposure was an industrial accident involving cyanogen bromide and one other was an unknown product. Doses of hydroxocobalamin ranged from 5-20 g, beginning a median 2.1 hours after cyanide ingestion or inhalation. Ten patients survived and were discharged. Seven of 11 patients who had potentially lethal blood cyanide levels survived. This survival rate compares favorably with that of smoke inhalation victims, and is further evidence that hydroxocobalamin provides clear benefits, particularly when administered before onset of cardiac arrest leading to anoxic brain damage. Limitations of this study were its retrospective nature and the lack of a comparison group, however the results supported the conclusion of safety and efficacy from other studies.

Case studies - cyanogenic household items/plants

Geller et al. reviewed published case reports from 1969 to 2004 which included 33 patients ranging in age from 11 months to 17 years old, with accidental ingestion of cyanogenic household substances including acetonitrile-containing false fingernail remover, cassava and tapioca (plant-based foods), and laetrile tablets, as well as nitroprusside exposures.⁶ Of this group, only four received hydroxocobalamin, but most cases occurred before this compound was available. All four children cited recovered after their exposure. With this limited literature support and mention of an unpublished series of pediatric cases of smoke inhalation, hydroxocobalamin is said to be a useful alternative to the cyanide antidote kit for acute cyanide poisoning in pediatric patients.

Bromley et al. reviewed a case report of a woman who accidentally poisoned herself and required hydroxocobalamin treatment.¹⁸ She was a cancer patient and was taking ascorbic acid 4.8 g/day along with other supplements. She then added amygdalin which she purchased over the Internet and took a single dose of 3 g approximately 30 minutes prior to becoming ill. When she presented 2½ hours later with classic symptoms of cyanide poisoning (seizures, severe lactic acidosis, intubated) she was given a single 5 g dose of hydroxocobalamin. Her symptoms reversed within hours and she was discharged two days later. Her estimated ingestion was 180 mg cyanide, well over the potentially lethal dose of 50-100 mg as hydrogen cyanide.

ADVERSE EFFECTS AND PRECAUTIONS

Serious adverse reactions with hydroxocobalamin include allergic reactions and increases in blood pressure. Many individuals with cyanide poisoning will be hypotensive however, so this reaction is potentially beneficial rather than detrimental to the patient. Elevations in blood pressure (to >180 mmHg systolic or >110 mmHg diastolic) were observed in approximately 18% of healthy subjects who were given 5 g and 28% of those given 10 g hydroxocobalamin.¹⁵ Increases in blood pressure were noted shortly after the infusion was started, with maximal effects at the end of the infusion. These elevations were generally temporary and returned to normal 20 minutes to four hours after the end of the infusion. Allergic reactions in two individuals were managed with antihistamines, while one case required parenteral corticosteroids.

TABLE 2. INCIDENCE OF ADVERSE REACTIONS OCCURRING IN >5% OF SUBJECTS IN 5 G DOSE GROUP AND CORRESPONDING INCIDENCE IN 10 G DOSE GROUP AND PLACEBO

Adverse drug reaction	5 g Dose Group		10 g Dose Group	
	Hydroxocobalamin n=66 n (%)	Placebo n=22 n (%)	Hydroxocobalamin n=18 n (%)	Placebo n=6 n (%)
Chromaturia (red colored urine)	66 (100)	0	18 (100)	0
Erythema	62 (94)	0	18 (100)	0
Rash*	13 (20)	0	8 (44)	0
Blood pressure increased	12 (18)	0	5 (28)	0
Nausea	4 (6)	1 (5)	2 (11)	0
Headache	4 (6)	1 (5)	6 (33)	0
Lymphocyte percent decreased	5 (8)	0	3 (17)	0
Infusion site reaction	4 (6)	0	7 (39)	0

* Rashes were predominantly acneiform and developed 7-25 days later, resolving in 6-38 days

Clinical Studies Experience

Because clinical trials were conducted under widely varying conditions, adverse reaction rates observed in the clinical trials may not reflect the rates observed in practice.

Experience in Healthy Subjects

A double-blind, randomized, placebo-controlled, single-ascending dose (2.5, 5, 7.5, and 10 g) study was conducted to assess the safety, tolerability, and pharmacokinetics of hydroxocobalamin in 136 healthy adult subjects.¹⁵ Because of the dark red color of hydroxocobalamin, the two most frequently occurring adverse reactions were chromaturia (red-colored urine) which was reported in all subjects receiving a 5 g dose or greater, and erythema, which occurred in most subjects receiving a 5 g dose or greater. Adverse reactions reported in at least 5% of the 5 g dose group and corresponding rates in the 10 g and placebo groups are shown in Table 2.

In this study, the following adverse reactions were reported to have occurred in a dose-dependent fashion and with greater frequency than observed in placebo-treated cohorts: increased blood pressure (particularly diastolic blood pressure), rash, nausea, headache and infusion site reactions. All were mild to moderate in severity and resolved spontaneously when the infusion was terminated or with standard supportive therapies. Only one patient of 136 had the infusion discontinued because of an allergic reaction.

Other adverse reactions reported in this study and considered clinically relevant included swelling, irritation and redness of the eye, dysphagia, abdominal discomfort, vomiting, diarrhea, dyspepsia, red blood in the stool, peripheral edema, chest discomfort, allergic reactions, memory impairment, dizziness, restlessness, dyspnea, throat tightness, dry throat, urticaria, pruritus and flushing.

Four open-label, uncontrolled, clinical studies (one of which was prospective and three of which were retrospective) were conducted in known or suspected cyanide-poisoning victims.^{3,10,11} A total of 245 patients received hydroxocobalamin treatment in these studies. Systematic collection of adverse event data was not done in all of these studies, and interpretation of causality is limited due to the lack of a control group and due to circumstances

of administration (e.g., use in fire victims). Adverse reactions reported in these studies which were not seen in healthy volunteers included ventricular extrasystoles, electrocardiogram repolarization abnormality, increased heart rate and pleural effusion.¹

Overdose

No data are available about overdose with Cyanokit in adults. Should overdose occur, treatment should be symptomatic. Hemodialysis may be effective but is only indicated in the event of significant hydroxocobalamin-related toxicity.¹

DRUG AND LABORATORY TEST INTERACTIONS

No formal drug interaction studies have been conducted with hydroxocobalamin as found in Cyanokit. Exercise caution when administering other cyanide antidotes simultaneously with hydroxocobalamin because the safety of coadministration has not been established. If a decision is made to administer another cyanide antidote with hydroxocobalamin, do not administer these drugs concurrently using the same IV line. Chemical incompatibility has been shown with sodium thiosulfate and sodium nitrite.^{1,2}

It is expected that multiple drugs would be administered to patients in conjunction with hydroxocobalamin as part of ACLS protocols. These would include but not necessarily be limited to sodium bicarbonate, epinephrine, antiarrhythmics, and anticonvulsants.^{7,8,19,20} It is recommended that these and other drugs/IV fluids be given in separate lines and alternate sites whenever possible. Physical incompatibility (particle formation) was observed with the mixture of hydroxocobalamin and the following: diazepam, dobutamine, dopamine, fentanyl, nitroglycerin, and propofol. These drugs require a separate line for administration. It is also recommended that blood products be infused through a separate IV line and alternate extremity if possible.¹

Because of its deep red color, hydroxocobalamin has been found to interfere with colorimetric determination of certain lab tests. The extent and duration of this interference depend on numerous factors including dose of the drug, methodology, analyzer and time between sampling and measurement. Because of this, caution should be used when reporting and interpret-

TABLE 3. LABORATORY INTERFERENCE OBSERVED WITH IN VITRO SAMPLES OF HYDROXOCOBALAMIN^{a1}

Laboratory parameters	No interference observed	Artificially increased ^a	Artificially decreased ^a	Unpredictable	Duration of interference
Clinical chemistry	Calcium Sodium Potassium Chloride Urea GGT ^b	Creatinine Bilirubin Triglycerides Cholesterol Total protein Glucose Albumin Alkaline phosphatase	ALT Amylase	Phosphate Uric acid AST Creatine kinase CKMB ^b LDH ^b	24 hours with the exception of bilirubin (up to 4 days)
Hematology	Erythrocytes Hematocrit MCV ^b Leukocytes Lymphocytes Monocytes Eosinophils Neutrophils Platelets	Hemoglobin MCH ^b MCHC ^b Basophils			12 to 16 hours
Coagulation				aPTT ^c PT ^c (Quick or INR ^c)	24 to 48 hours
Urinalysis		pH (with all doses) Glucose Protein Erythrocytes Leukocytes Ketones Bilirubin Urobilinogen Nitrate	pH (with equivalent doses of <5 g)		48 hours up to 8 days; color changes may persist up to 28 days.

^a≥10% interference observed on at least 1 analyzer. Analyzers used: **ACL Futura** (Instrumentation Laboratory), **AxSYM/Architect** (Abbott), **BM Coasys¹¹⁰** (Boehringer Mannheim), **CelIDyn 3,700** (Abbott), **Clinitek 500**(Bayer), **Cobas Integra 700, 400** (Roche), **Gen-S Coultronics**, **Hitachi 917**, **STA Compact**, **Vitros 950**(Ortho Diagnostics).

^bGGT = gamma glutamyltransferase; CKMB = creatine kinase isoenzyme MB;LDH = lactate dehydrogenase; MCV = mean cell volume; MCH = mean cell hemoglobin; MCHC = mean cell hemoglobin concentration.

^caPTT = activated partial thromboplastin time; PT = prothrombin time; INR = international normalized ratio.

Copied from package insert, 12/06¹

ing laboratory results. Table 3 is for interference after a 5 g dose. Interference after a 10 g dose could last up to an additional 24 hours.

In a two-part study (in vivo and in vitro) done with rabbits, it was shown that hydroxocobalamin caused optical interference with cooximetry measurements of total hemoglobin (tHb), carboxyhemoglobin (COHb), methemoglobin (MetHb), and oxyhemoglobin (Hb-O₂) in blood. These effects are especially important in management of smoke inhalation victims who would have also been exposed to carbon monoxide. While the results were limited, this study indicated falsely elevated levels of COHb, MetHb and Hb-O₂ can occur in clinical situations.²¹

DOSE AND HOW SUPPLIED

Hydroxocobalamin for use in the treatment of cyanide poisoning is dosed as an initial 5 g dose in adults, to be administered intravenously over 15 minutes. Each kit contains two vials of 2.5 g apiece, so both vials need to be administered for a single dose. Each vial must be reconstituted with 100 mL of normal saline (0.9% sodium chloride injection). Alternate infusion fluids include 5% Dextrose injection (D5W) or Lactated Ringers injection. Following dilution the vials need to be inverted and rocked, not shaken, for at least 30 seconds prior to infusion. Depending on the response of the patient, a second dose of 5 g may need to be administered. Total doses of up to 15 g have been reported in

the literature. This product should be kept at controlled room temperature, although diversions from this are allowed (see stability information in Summary).

For pediatric patients a dose of 70 mg/kg has been used and is the licensed pediatric dose in France.^{1,6} In a review of 32 cases of children exposed to cyanide in a variety of settings, hydroxocobalamin was given in four cases.⁶ In limited clinical experience serious adverse effects have not been reported and the drug was well tolerated.

CONCLUSION

Hydroxocobalamin appears to have no major toxicities. Its risk-benefit profile supports use in both pre-hospital and hospital settings.¹¹ It could potentially revolutionize the management of acute cyanide poisoning by facilitating rapid pre-hospital intervention.^{20, 22} The ability to use a cyanide antidote empirically at a fire or disaster scene could significantly improve patient outcomes. Also, hydroxocobalamin need not be reserved for cases of confirmed cyanide poisoning but could be administered in cases of suspected exposure (fire victims).

Stocking quantities must consider management of several victims at one time. Consider that victims may have received one dose in the field if and when paramedic ambulances start to carry this product. One kit consists of two vials and the entire contents are needed for a single adult dose. A maximum of two kits (10 g) would be expected to be used in a single adult patient. For pediatric patients, one vial (2.5 g) would be sufficient for up to a 78 pound individual at a dose of 70 mg/kg. This is not a drug that can be ordered when needed but must be on hand when exposures are being managed. The expiration date of the Cyanokit is 30 months from time of production. ●

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Pet Prescription Taxation as Defined by the Wisconsin Dept. of Revenue

by Katie Holmes

Logic suggests that pharmacy laws should most commonly exist under Chapter 450 of Wisconsin Pharmacy Laws, the Wisconsin Controlled Substances Act, Chapter 961, or rules of the Pharmacy Examining Board. However, we cannot overlook Wisconsin laws that apply to the practice of pharmacy that are defined outside of these statutes.

State legislation regarding taxable sales of medicines for animal use has recently been examined with respect to its impact on pharmacies. The Wisconsin Department of Revenue defines retail sales of medicines for pets as taxable purchases under State Sales Tax Code 11.09(5b). Additionally, the sale of pharmaceuticals to veterinarians is a taxable sale to the veterinarian according to State Sales Tax Code 11.61(2a). Medicines for pets to be used or furnished by veterinarians in the performance of their professional services to animals shall be subject to state sales tax. If a prescription is for a livestock animal, it is considered non-taxable; however the farmer must present a sales tax exemption certificate to prove tax exempt status. The only exemption for veterinarian purchases shall be in the case of medicines purchased for use in farm livestock.

These sales tax laws may be new information for some pharmacists since there is generally a sole emphasis placed upon pharmacists thoroughly knowing and understanding the Wisconsin pharmacy laws detailed in chapter 450 and chapter 961, as well as those defined by the Pharmacy Examining Board. Even though this information is not included in the state statutes that pharmacists have come to know so well, this law still governs a specific aspect of pharmacy practice. For this reason, it is prudent to examine your pharmacy practice to ensure it complies with the state sales tax code for animal prescriptions.



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