Recommendations for Managing Toxic Alcohols during the Fomepizole Shortage

Toxic alcohols most commonly ingested and treated in the hospital setting include ethylene glycol (radiator fluid) and methanol (commonly windshield washer fluid, among other sources). Toxic alcohols lead to a severe anion-gap metabolic acidosis as they are metabolized by alcohol dehydrogenase and then further by aldehyde dehydrogenase to form the toxic acid metabolites oxalic acid from ethylene glycol and formic acid from methanol. Ultimately, severe ingestions left untreated will lead to death, but if survived may cause morbidity including renal failure, blindness, and severe permanent CNS dysfunction.

The antidote fomepizole (Antizol®) blocks the enzyme alcohol dehydrogenase and prevents the formation of dangerous acid metabolites while the toxic alcohol is excreted (several days depending on level) or more commonly, dialyzed. There is currently a shortage of fomepizole nationwide and is unclear when this shortage will end. The only alternative to blocking alcohol dehydrogenase is through ingestion of ethanol, for which the enzyme has a higher affinity. Any patient suspected of ingesting a toxic alcohol should be treated while waiting for results of blood analysis (please contact the Kentucky Regional Poison Control Center for Assistance – do not use send out labs as these will not return levels in time to make clinical judgments).

Please note, isopropyl alcohol is not metabolized to acid metabolites and its metabolism does not need to be blocked.

- The 5% and 10% ethanol solutions are no longer available. It is **not** recommended that IV ethanol be compounded except under extreme circumstances.
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- Therefore, the recommendation is that the patient be provided **oral ethanol**.

- We recommend the pharmacy stock vodka until fomepizole can be obtained. Vodka is 40% (80 proof) and can be diluted to make a 20% solution for ingestion.

- Although oral absorption is variable and dependent on several factors, appropriate levels can usually be achieved at 0.8 grams/kg (4 ml/kg of a 20% solution) administered over 20 minutes. Frequent blood alcohol levels should be monitored and ethanol titrated to maintain a BAL of 100 mg/dl to 150 mg/dl to prevent the production of toxic alcohol metabolites.

- (See the dosing chart below: ***Nelson, Lewin, Holland, et.al. Goldfrank's Toxicologic Emergencies. Ninth Ed. 2011. McGraw-Hill; New York, NY: 1420-1421***.)

TABLE A32–2. Oral Administration of 20% Ethanol

	Volume (mL)					
Loading Dose[a]	**10 kg**	**15 kg**	**30 kg**	**50 kg**	**70 kg**	**100 kg**
0.8 g/kg of 20% ethanol, diluted in juice (may be administered orally or via nasogastric tube)	40	60	120	200	280	400
	mL/h for various weights[c,d]					
Maintenance Dose[b]	**10 kg**	**15 kg**	**30 kg**	**50 kg**	**70 kg**	**100 kg**
Ethanol naive						
80 mg/kg/h	4	6	12	20	28	40
110 mg/kg/h	6	8	17	27	39	55
130 mg/kg/h	7	10	20	33	46	66
Ethanol tolerant						
150 mg/kg/h	8	11	22	38	53	75
During hemodialysis						
250 mg/kg/h	13	19	38	63	88	125
300 mg/kg/h	15	23	46	75	105	150
350 mg/kg/h	18	26	53	88	123	175

[a] A 20% V/V concentration yields approximately 200 mg/mL.

[b] Concentrations above 30% (60 proof) are not recommended for oral administration. The dose schedule is based on the premise that the patient initially has a zero ethanol concentration. The aim of therapy is to maintain a serum ethanol concentration of 100 to 150 mg/dL, but constant monitoring of the ethanol concentration is required because of wide variations in endogenous metabolic capacity. Ethanol will be removed by hemodialysis, and the dose of ethanol must be increased during hemodialysis. Prolonged ethanol administration may lead to hypoglycemia.

[c] Rounded to the nearest mL.

[d] For a 30% concentration, multiply the amount by 0.66.

Adapted from Roberts JR, Hedges J, eds. *Clinical Procedures in Emergency Medicine*. Philadelphia: WB Saunders; 1985:1073-1074.

- You should <u>not wait</u> until fomepizole is needed to obtain and stock oral alcohol.
- If necessary, administer alcohol through a nasogastric tube.
- In extreme circumstances (current gastric bleeding or concomitant caustic ingestion) consideration could be given to compounding ethanol for IV use. The following compounding instructions are found in *Goldfrank's Toxicologic Emergencies* (see reference above).

Ethanol Preparation for Toxic Alcohols (Not Recommended Unless No Alternative)

Preparation for 10% Ethanol in D5W:

Ingredients:

- sterile ethanol USP (100% ethanol)
- Dextrose 5% 500 mL

Steps

1. Draw up 55 mL of ethanol USP
2. Inject 55mL ethanol USP into 500 mL bag of dextrose 5%
3. Label bag as "Ethanol 10% = 55mL/555mL"
4. Label with expiration date of 24 hours from time of preparation

Administration:

Central line only

Duration:

Treatment should continue until serum toxic alcohol concentration < 20-25 mg/dL

Y-site Compatibility:

Limited information available regarding Y-site co-administration

TABLE A32–1. Intravenous Administration of 10% Ethanol

	Volume (mL)[b] (given over 1 h as tolerated)					
Loading Dose[a]	10 kg	15 kg	30 kg	50 kg	70 kg	100 kg
0.8 g/kg of 10% ethanol (infused over 1 h as tolerated)	80	120	240	400	560	800
	Infusion Rate[b] (mL/h for various weights)[d]					
Maintenance Dose[c]	10 kg	15 kg	30 kg	50 kg	70 kg	100 kg
Ethanol Naive						
80 mg/kg/h	8	12	24	40	56	80
110 mg/kg/h	11	16	33	55	77	110
130 mg/kg/h	13	19	39	65	91	130
Ethanol Tolerant						
150 mg/kg/h	–	–	–	75	105	150
During hemodialysis						
250 mg/kg/h	25	38	75	125	175	250
300 mg/kg/h	30	45	90	150	210	300
350 mg/kg/h	35	53	105	175	245	350

[a] A 10% V/V concentration yields approximately 100 mg/mL.

[b] For a 5% concentration, multiply the amount by 2.

[c] Infusion to be started immediately following the loading dose. Concentrations above 10% are not recommended for IV administration. The dose schedule is based on the premise that the patient initially has a zero ethanol concentration. The aim of therapy is to maintain a serum ethanol concentration of 100 to 150 mg/dL, but constant monitoring of the ethanol concentration is required because of wide variations in endogenous metabolic capacity. Ethanol will be removed by hemodialysis, and the infusion rate of ethanol must be increased during hemodialysis. Prolonged ethanol administration may lead to hypoglycemia.

[d] Rounded to the nearest mL.

Adapted from Roberts JR, Hedges J, eds. *Clinical Procedures in Emergency Medicine*. Philadelphia: WB Saunders; 1985:1073-1074.